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No. 1

SUMMARY OF FOUR YEARS OF CLINICAL AND BACTERIOLOGIC EXPERIENCE WITH MENINGITIS IN NEW YORK CITY *

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NEW YORK

July 1, 1910, the preventive medicine annex of the Research Laboratory of the New York Board of Health took over the preparation, distribution and administration of antimeningitis serum from Rockefeller Institute. Jochmann, Kolle and Wassermann, the New York Board of Health and others had prepared the serum some time before it was taken up by Rockefeller Institute, so the serum itself was not new, but the credit for introducing its intraspinal use in this country is Dr. Flexner's. Under his direction, the Rockefeller Institute prepared it and distributed it to all who would supply careful records. This was of the greatest advantage in procuring a quick decision as to its great value. During part of the last big epidemic here (1904-05) the Health Department tried using it subcutaneously and found it to be of such doubtful value that its preparation was discontinued.

Meningitis is a reportable disease in New York City. The plan of the department from the first has been to have the physician on each case, so soon as he is known by the report of the case, offered the services of a department consultant.

We make our appointments with the attending physicians for the earliest moment possible and see cases nights and Sundays with them, because occasionally twelve hours' delay will seem to be a possible cause of a fatal outcome. We go over the history, examine the case, and if it seems to us to warrant it, even though we may not consider it to be one of meningitis, we do a lumbar puncture. It takes tact and infinite patience to persuade some of the poor, ignorant, foreign parents to allow us to do it, but usually if properly approached, they finally give in.

The conditions we have to consider mainly are epidemic or meningococcic meningitis, other purulent meningitides due most commonly in our experience to the streptococcus and pneumococcus and less

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* From the Research Laboratory, Department of Health, New York City.

commonly to the *Streptococcus mucosus capsulatus* and influenza, tuberculous meningitis, poliomyelitis and meningism, particularly in pneumonia. We see many other conditions, as our yearly tabulations will show — sufficient, indeed, to make our work pleasantly exciting, for when a case is reported the probabilities are that it is not going to be epidemic cerebrospinal meningitis.

As a general thing, we do not go to see patients in hospitals. At first we thought such cases received proper treatment and did not need us, but as our knowledge of meningitis has increased and we have from time to time had occasion to observe such treatment and the results, we think hospitals would be wise to call us in once in a while to instruct the house staffs, for they are often left pretty much to their own devices, and though the serum treatment of meningitis is beginning to find its way into text-books the busy attending physicians have not had much occasion to learn about it and have little advice to offer.

The points of differentiation in their order of value among the above named conditions are in general, lumbar puncture with the examination of the fluid, the history and the physical signs.

A clear fluid increased in amount indicates usually one of the following conditions: tuberculous meningitis, poliomyelitis, syphilitic involvement of the central nervous system, brain tumor or meningismus. A cloudy fluid is the result of a meningitis due to the meningococcus or some of the other pyogenic organisms.

In examining fluids, we make both bacteriologic and chemical studies and when these are not conclusive inoculate guinea-pigs. We make smears and cultures from the sediment if fluids contain any. Other fluids are centrifuged for one hour at high speed and the smear made by putting the last few drops from the tube onto a slide and evaporating to dryness in the incubator. Smears from cloudy fluids are stained by Gram's method, those from clear fluids with Ziehl's tubercle bacillus stain. Occasionally it is necessary to make a capsule stain. In examining the smears we note the presence or absence of bacteria and the number and kinds of cells.

We have never counted the cells for two reasons: first, it is some time usually between the time fluids are withdrawn and the time that they are examined, for most cases are at some distance from the laboratory; secondly, we see no great advantage in doing it. We can tell from the stained sediment whether the cells are increased much, little, or not at all, and there is nothing particularly diagnostic in the exact number of cells per cubic millimeter. Moreover, since in most cases the cells are very few in number and it is impossible to use a large amount of fluid, no method can be very accurate. In poliomyelitis at the stage at which we usually see it, and in tuberculous and syphilitic

meningitis, the cells are considerably increased, there being from 20 to 30 to a field. Mononuclears predominate up to 95 per cent. often. In epidemic cerebrospinal meningitis and the meningitides due to other pyogenic organisms the cells are enormously increased, so much so that it is not necessary to centrifuge. The polymorphonuclear leukocytes predominate, often up to 98 per cent. at first. Later, if the condition improves, the cells decrease and gradually the percentage of mononuclears increases.

The cultures are made after the smears are examined. Those showing *Streptococcus pyogenes*, *Streptococcus mucosus capsulatus* or meningococcus, or those in which no organism is found, but one of these is suspected of being the cause, are planted on 2 per cent. glucose ascitic agar. Those showing influenza or pneumococcus are planted on blood agar. Clear fluids are always injected subcutaneously in from 5 to 7 c.c. amounts into the groins of a guinea-pig. The pig is kept for a month and then injected in the axilla with 1 c.c. of crude tuberculin diluted to 3 c.c. with normal saline. Usually if it is tuberculous it is dead next morning. For proof of tuberculosis we depend on caseous inguinal glands or tubercles in the spleen or both at necropsy. Clear fluids that have become contaminated will sometimes produce enlarged inguinal glands that may even go on to caseation, but 1 c.c. of tuberculin will not kill in those cases.

We make chemical tests for albumin, globulin and reduction with Fehling's solution. For albumin, we use the nitric acid ring test and judge of the amount of albumin by the depth of the ring when it is first formed. The globulin test is that of Noguchi and is made by adding to one part of the fluid four or five parts of 10 per cent. butyric acid made up in normal saline, boiling, adding about as much normal sodium hydroxid as there was fluid to begin with and boiling again. Too much sodium hydroxid spoils the test by redissolving the globulin. Normal fluids will give a very faint opalescence; pathologic fluids a flocculent precipitate varying in amount with the severity of the inflammation present. Fluids showing globulin are said to be the result of inflammation of the meninges and we have never had reason to doubt it. Indeed, to us it is the most important of the chemical tests, because it separates fluids due to meningism from those due to a true meningeal infection. Both the albumin test and the globulin test are of course worthless, if there is blood present. The majority of clear fluids reduce Fehling's solution. The statement is now and then made that a differential point in diagnosis between tuberculous meningitis and poliomyelitis is the fact that poliomyelitis fluids will reduce Fehling's solution, but tuberculous fluids will not. We have tried Fehling's reaction with eighty-eight known tuberculous fluids and sixty-five, or 73 per

cent., gave good reduction. So, while the absence of reduction is of marked significance, the presence of reduction means absolutely nothing. The fluid from a case of heat prostration also failed to reduce Fehling's. In cloudy fluids it is not uncommon to find the reduction present if the case is seen early and is mild, then to go through a period where there is no reduction, and as the patient improves and the fluid clears, to have it return. In making the test we use equal quantities of Fehling's solution and spinal fluid.

We have examined two fluids and have seen a third that illustrated the syndrome of Froin. This is characterized by spontaneous coagulation and a yellow color. The pathogenesis of this condition is not known except, of course, that some hemorrhage has taken place. The two fluids we examined were from poliomyelitis patients, one of whom recovered and one died. The third fluid was from a patient with epidemic cerebrospinal meningitis supposed to have had a fracture of the skull. This patient recovered.

Table 1 is a concise statement of the various characteristics of the different fluids.

From July 1, 1910, to July 1, 1914, we examined 992 cerebrospinal fluids. Included with those we withdrew are some sent in by physicians who made their own punctures. Our method of examination and the differential points have already been discussed. We have found that examinations of fluids from epidemic cerebrospinal meningitis are more apt to be successful if done promptly, as the meningococcus sometimes autolyzes in twelve hours so that they will not grow and are very difficult to distinguish by smear. As cases recover the organisms are found more and more within the cells, and they usually show in spreads after the cultures become negative.

In examining for tubercle bacilli, we find the sediment after prolonged centrifuging at high speed better adapted to our purposes than the examination of the fibrin web. As our fluids are brought to the laboratory from varying distances, the formation of the web is disturbed; frequently, too, we wish to examine a fluid without allowing time for the web to form. By this method we get positive results in about 65 per cent. of cases. This is not nearly so high a percentage as that obtained by Dr. Hemingway at the Babies' Hospital using the web, but she was able to make several punctures, if necessary, while we rarely see a case of tuberculous meningitis more than once.

The history is of importance in the purulent meningitides, for, though they are differentiated from each other only by microscopical and cultural examinations, a history of middle-ear disease or fracture of the skull makes us suspect that some other than the meningococcus is the infecting organism. In differentiating between tuberculous

meningitis and poliomyelitis the history is of more importance than the examination of the spinal fluid if tubercle bacilli are not found, because the chemical and microscopic pictures are so frequently identical in the two conditions. In poliomyelitis there is usually the history of a sudden onset with a very high temperature dropping quickly. There may have been prodromata; gastro-intestinal disturbance is common, and many cases show redness of the throat or some involvement of the upper respiratory tract, but they are so slight that it takes careful questioning to elicit them. The history of a tuberculous case, on the other hand, is usually that of an insidious onset preceded by unusual irritability, though occasionally we see children in families in which they have been carefully observed that give a history of a sudden onset, frequently with convulsions. Usually the temperature has been between 99 and 101 F.; occasionally it will have been normal or subnormal. Transient paralyses, projectile vomiting and crying out in the night are frequently mentioned. Given a patient in apparent coma, usually a determined effort will rouse the child with poliomyelitis and he will answer intelligently, though afterward he sinks back immediately into stupor. It is impossible to rouse the tuberculous child in the stuporous stage.

The differentiation between epidemic cerebrospinal meningitis and tuberculous meningitis is usually comparatively easily made. Cases of epidemic cerebrospinal meningitis usually give a history of a sudden onset as against a slower onset in tuberculous meningitis. The patient's mental condition usually remains good in meningococcic meningitis unless it is a fulminating case. In tuberculous meningitis the history is commonly that of irritability followed by increasing stupor from which it is impossible to arouse the child. Patients with epidemic cerebrospinal meningitis show marked rigidity of the neck; tuberculous patients are apt to have slight or moderate anterior-posterior rigidity, but none laterally. In infants the rigidity of epidemic cerebrospinal meningitis is so easily overcome as to make one often doubt its existence, but when the infant is turned on the side the head is markedly retracted. The fever is higher in epidemic cerebrospinal meningitis, and runs an irregular course. Projectile vomiting is common in tuberculous meningitis and rare in epidemic meningitis.

Very few luetic or other chronic conditions of the central nervous system or meninges come to our attention, but we do see a good many cases of meningism. By meningism we mean that condition in which meningeal symptoms arise in the course of some disease, the cerebrospinal fluid being increased in amount but normal in character. Some difference of opinion exists in regard to the use of the term. It was introduced by Dupré, who considered it a functional disturbance.

Other writers have used the term serous meningitis, pseudomeningitis, meningitis sine meningitide and meningitis infectiosa circumscripta or circumscribed meningitis. This latter term is considered preferable by Plant, Rehm and Schottmüller. Holt describes a case which showed at necropsy a circumscribed meningitis. Huber in an article on "Pneumococcus Meningitis and Meningism," inclines to the opinion that the pathologic basis is a localized inflammation, usually of infectious origin.

In the face of this evidence we cannot deny that cases exist in which the clinical picture and the increased fluid is due to a circumscribed infection, but from our experience it seems to us highly improbable that this is always or even often the case.

We have seen 80 cases of which the outcome in 53 was recovery and in 22 death, while with 5 the outcome is unknown. The diseases which the meningism accompanied are as follows:

| | |
|--|----|
| Pneumonia—uncomplicated | 39 |
| Gastro-intestinal disease | 8 |
| Whooping-cough (two patients had pneumonia also) | 6 |
| Scarlet fever (one patient had pneumonia also)... | 5 |
| Typhus | 3 |
| Typhoid complicated by pneumonia | 1 |
| Measles | 1 |
| Middle-ear disease | 1 |
| Retropharyngeal abscess | 1 |
| Orbital abscess | 1 |
| Pott's disease | 1 |
| Epilepsy | 1 |
| Rachitis | 1 |
| Streptococcus osteomyelitis | 1 |
| Staphylococcus septicemia | 1 |
| Influenza | 1 |
| Nephritis | 1 |
| Heat prostration | 1 |

Of the 22 patients who died, 8 died within twenty-four hours, and were desperately ill when seen. Of the 14 living longer than twenty-four hours, 4 died of pneumonia (in 1 two punctures were made with normal fluid in each instance), 1 of gastro-intestinal disease, 1 of whooping-cough complicated with bronchopneumonia, 3 of scarlet fever (1 complicated by bronchopneumonia and diphtheria, and 1 very septic), 1 of typhoid complicated by pneumonia, 1 of staphylococcus septicemia (two punctures done with normal fluid, one of streptococcus osteomyelitis—necropsy showed normal brain and meninges), 2, cause unknown.

In most of these cases the meningeal symptoms did not progress. Had they done so, a second puncture would have been made. In two cases, as noted, second punctures were done revealing normal fluids. In all cases the severity of the accompanying disease or diseases was quite sufficient to account for death. Of course, this by no means proves the absence of a localized meningeal infection. We have never

seen a case of generalized meningitis following a case of meningism, however, which we should expect to see occasionally considering the number under observation, were there a localized infection of the meninges, and in view of the relatively large number of patients that recover promptly, we believe that in most cases the condition is a functional one, probably of toxic origin.

In sixty-nine of these cases lumbar puncture was done. In the other cases we did not do a puncture, either because the symptoms had cleared up considerably when the case was seen or because with the accompanying disease we felt sure the case was one of meningism and advised waiting. Latterly, we have done a lumbar puncture even though we have felt sure it was meningism, as the withdrawal of the fluid seems to hasten recovery.

Of course, the amount of fluid depends on the stage of the condition at which the puncture is done. We have withdrawn very large amounts—from 80 to 100 c.c. In other cases the amount has been little increased above normal. It is commonly accepted that in a true meningitis the fluid is inflammatory in character—of the nature of an exudate. Such a fluid shows an increase in albumin and globulin and in the number of cells. In a meningism, as we use the term on the other hand, the fluid is of the nature of a transudate. Except in the cases noted below, the cells have not been increased, neither has the albumin and globulin content, and Fehling's has been readily reduced. In all cases they have been negative bacteriologically, by smear culture and animal inoculation.

In two cases of pertussis, the patients dying the same day the puncture was done, there was some increase in albumin and globulin and number of cells, in one case about equally divided between endothelial cells and polynuclears, in the other 95 per cent. or more polynuclears. These changes were presumably ante mortem. In one case of typhus the cells were increased—95 per cent. mononuclears. This patient recovered. The case of heat prostration showed a faint increase in albumin and a slight increase in cells, 70 per cent. being polynuclears. This fluid, as has been stated before, failed to reduce Fehling's, though repeated tests were made, and was the only fluid that did not do so readily. The patient recovered.

Plaut, Rehm and Schottmüller include under the term "meningism" cases with spinal fluid in which there is an increase in albumin and globulin and in number of cells usually mononuclear, sometimes polynuclear. We feel that such instances may be mild and recovering cases of epidemic cerebrospinal meningitis in which the organism has cleared up before the puncture was made. We have seen several cases ourselves in which from the clinical history, the progress of the case and

the character of the fluid we were convinced of the diagnosis, while we were unable to prove it bacteriologically.

In examining patients, we particularly note the following points: the presence or absence of MacEwen's sign or in infants a bulging fontanelle; the eyes (whether or not the pupils are dilated, contracted or unequal, presence of conjunctivitis, strabismus, nystagmus, etc.); the mental condition (whether there is delirium, irritability or stupor); the presence or absence of Kernig's and Brudzinski's signs; regularity in rate and depth of respiration and rate and volume of pulse; the reflexes (whether they are increased, diminished or absent); the temperature and presence or absence of an eruption. Of these signs we consider the stiffness of the neck, the variation of regularity in rate and

TABLE 1.—CHARACTERISTICS—

| Meningeal Condition | Pressure | Amount c.c. | Appearance | Cytology |
|-----------------------------------|-----------|-------------|------------------------------------|--|
| Normal | Normal | 5-10 | Clear | Very few cells |
| Meningismus | Increased | 10-100 | Clear | Very few cells |
| Poliomyelitis | Increased | 20-100 | Clear; sometimes slight fibrin web | Early polynucleosis; later lymphocytosis up to 95 per cent.; endothelial cells |
| Tuberculous meningitis | Increased | 30-120 | Clear fibrin web | Lymphocytosis up to 95 per cent. |
| Epidemic cerebrospinal meningitis | Increased | 5-120 | Cloudy | Polynucleosis up to 98 per cent. |
| Meningitis due to other organisms | Increased | 20-100 | Cloudy | Polynucleosis up to 98 per cent. |

depth of respiration and MacEwen's and Brudzinski's signs the most important. MacEwen's sign consists of a change from the normal in the percussion note over the lateral ventricles due to increased intraventricular pressure. It takes some practice to appreciate it. Brudzinski's sign consists in the flexion and eversion of the legs and arms when an attempt is made to flex the head on the chest. Wherever we have found a MacEwen we have always obtained increased fluid, except in cases of basilar meningitis, in which case the connection between the brain and cord is partially or totally cut off.

The mental condition is frequently good in epidemic cerebrospinal meningitis unless the case is of the fulminating type. Early in tuberculous meningitis there is irritability, later stupor. In poliomyelitis irritability not followed by stupor is the usual thing.

Conjunctivitis is fairly common in epidemic cerebrospinal meningitis and rare in other meningeal conditions. Ptosis and strabismus are

more common in tuberculous meningitis, but may occur in other meningeal conditions.

We do not attach much significance to Kernig's sign, because it is difficult to make sure of it in young children. Brudzinski's sign is of much greater value to our minds.

In true meningitis the depth and time between respirations is markedly irregular, the so-called Biot's breathing. Late, particularly in tuberculous meningitis, the respiration frequently becomes Cheyne-Stokes. The pulse is more apt to be irregular in rate and volume in tuberculous meningitis than in other meningeal conditions.

Palsies are uncommon in epidemic cerebrospinal meningitis; in 112 cases we have seen palsy twice only. It is common, but usually transi-

—OF THE VARIOUS FLUIDS

| Bacteriology | Albumin | Globulin | Fehling's Solution | Animal Inoculation |
|--------------------|---------|----------|--|----------------------------|
| Sterile | ± | ± | + | Negative |
| Sterile | ± | ± | + | Negative |
| Sterile | +—++ | +—++ | + | Negative |
| Tubercle bacilli | ++—++++ | ++—++++ | — in 25 per cent. | Tuberculosis in four weeks |
| Meningococcus | ++—++++ | ++—++++ | + or — according to severity and stage | |
| Infecting organism | ++—++++ | ++—++++ | — may be + early | |

tory in tuberculous meningitis, and always present in frank cases of poliomyelitis.

As has already been stated, the temperature in general is low and long continued in tuberculous meningitis, is high, rising rapidly and dropping quickly in poliomyelitis and runs a very irregular course in epidemic cerebrospinal meningitis.

Eruptions aside from herpes are not very common in our experience, though in times past epidemic cerebrospinal meningitis has been known as spotted fever. In 112 cases we have seen an eruption sixteen times. In cases in which it did occur there was nothing characteristic about the eruption itself, its location or the time of its appearance or disappearance.

Table 2 shows the number of cases from July 1 of one year to July 1 of the next year for the last four years.

The increase in numbers from year to year has been partly due to the gradual spread of the knowledge that such work is being done. We regret that even after four years there are many physicians in New York who are entirely unaware of the existence of our department. Aside from that, we feel that there has been a real increase in the number of cases of epidemic cerebrospinal meningitis. It is a disease for which apparently the majority of individuals have a natural immunity. Many healthy people carry meningococci in their noses and throats for long periods of time, acquiring them either from cases or from carriers. After a certain length of time, when there has been

TABLE 2.—NUMBER OF CASES BY YEARS, JULY 1, 1910, TO JULY 1, 1914*

| | 1910-1911 | 1911-1912 | 1912-1913 | 1913-1914 | Total |
|---|-----------|------------|------------|------------|------------|
| Epidemic cerebrospinal meningitis | 17 | 25 | 29 | 41 | 112 |
| Tuberculous meningitis.... | 22 | 44 | 37 | 51 | 154 |
| Other meningitides | 11 | 7 | 11 | 18 | 47 |
| Anterior poliomyelitis..... | 1 | 25 | 16 | 5 | 47 |
| Pneumonia | 6 | 8 | 16 | 22 | 52 |
| Other diseases | 14 | 30 | 20 | 53 | 117 |
| | <u>71</u> | <u>139</u> | <u>129</u> | <u>190</u> | <u>529</u> |

* Some few of the cases during the first two years were seen only by Dr. Sophian, who had charge of the work during that time.

TABLE 3.—NUMBER OF CASES DURING THE FOUR QUARTERS OF THE YEAR

| | July- October | October- January | January- April | April- June |
|-----------------|------------------|---------------------|-------------------|----------------|
| 1910-1911 | .. | 5 | 3 | 9 |
| 1911-1912 | 6 | 4 | 10 | 5 |
| 1912-1913 | 4 | 6 | 9 | 10 |
| 1913-1914 | 2 | 4 | 16 | 19 |
| | <u>12</u> | <u>19</u> | <u>38</u> | <u>43</u> |

little meningitis about, a new generation of susceptible individuals comes on the scene. These, with possibly certain meteorologic factors which we do not understand, probably determine epidemics to a large extent. It has been about ten years since the beginning of the last epidemic. With the increasing number of cases another epidemic may be approaching. Fortunately, this last year it has been of a mild type.

Table 3 gives the number of cases during the four quarters of each year. The greatest number of cases occurs between March 1 and June 1 each year.

Table 4 shows the number of physicians with whom we have consulted and the number of cases we have seen with each.

There are 531 instead of 529 cases, because in two instances there were two physicians in charge of cases, and in order to make the number of physicians come out right it was necessary to count each of these cases as two.

TABLE 4.—PHYSICIANS CONSULTED AND CASES SEEN

| Physicians | No. of Cases Seen with Each | No. of Cases Seen |
|------------|-----------------------------------|----------------------|
| 254 | 1 | 254 |
| 60 | 2 | 120 |
| 10 | 3 | 30 |
| 8 | 4 | 32 |
| 8 | 5 | 40 |
| 4 | 6 | 24 |
| 1 | 7 | 7 |
| 3 | 8 | 24 |
| <hr/> 348 | | <hr/> 531 |

The treatment of epidemic cerebrospinal meningitis resolves itself into prophylaxis and specific and general treatment. The prophylaxis consists in quarantining patients ill with the disease and those in contact with them who show meningococci in cultures from the nose and throat. Under ordinary circumstances epidemic meningitis is not very highly contagious, but it sometimes becomes so. We have seen more than one case in a family in only four instances. The first time a child of 11 had it and three months later her mother had it. Both recovered. The second time two brothers, adults, were sick in the same room. Most insanitary conditions prevailed. The first brother had been ill two weeks and had had no doctor. The second was a fulminating case and the patient died in three days. The first one was sent to a hospital and finally died after five weeks' illness. In the third instance, a brother and sister, adults, and the 8-year-old daughter of the sister were all ill in the same apartment. The brother and sister were taken ill within two hours of each other and both died. The little girl was taken five days later and recovered. The day before the little girl was taken sick a neighbor, a man living in the same house came down with it and eventually recovered. The fourth instance was that of a sister of 14 and a brother of 3½. The sister had been taken sick two days before the boy. The attacks were mild and both recovered.

The question of carriers is rather a difficult one. In the first place, it requires careful bacteriologic technic to isolate meningococci from nose and throat cultures when they are few in numbers, and the work cannot be left to laboratory assistants unless they have exceptional training. When there are many cases to be diagnosed and treated is the time when nose and throat cultures from carriers come in thick and fast, and until quite recently we have not had a sufficiently large force to manage the cultures satisfactorily. From some work done here two years ago, we think the most satisfactory method of dealing with carriers is to swab out the nose and throat two or three times daily with 20 per cent. argyrol. We hope to do more work along this line this winter. Hatchel and Hayward report success with a spray of anti-meningococcic serum and with subcutaneous injections of meningococcus vaccine.

The specific treatment consists in the intraspinal administration of antimeningitis serum. This is a specific immune serum of therapeutic value only in meningococcic meningitis and then only when administered subdurally. In making a lumbar puncture we do not use either general or local anesthesia. We think that general anesthesia is dangerous, and local anesthesia takes so much preparation and time that the overcoming of the pain does not compensate for the increased nervous tension on the part of the patient. Adults not acutely ill who submit to lumbar puncture for diagnostic purposes do not seem to mind much. The back is not very sensitive, and if the patient is held properly—lying on the side with the knees drawn up against the abdomen, the neck bent and the back well arched so that the intervertebral spaces will be as great as possible—and the operator is skilful there is very little pain. Never under any circumstances do we do it with the patient sitting up. Iodin is used over about 4 square inches immediately around the point of election for puncture and a sterile or bichlorid towel is laid over the hips through which to find the landmarks. We have never to our knowledge had a secondary infection of the meninges of the cord. Sometimes the skin has become infected in small children from soiled napkins. We use a Quincke needle size 18 or 19, and go in the mid-line through the notch most nearly coinciding with a line drawn from crest to crest of the ilium. A piece of tubing about 15 inches long is attached to the metal connection that fits in the end of the needle when the stylet is withdrawn. To the other end of the rubber tubing is attached the barrel of a syringe. We usually cut the rubber and insert a short piece of glass tubing near the metal connection so that we can see the fluid flowing out or the serum flowing in. It is well to attach the tubing in removing the fluid because by raising and lowering the glass container the

rapidity of outflow can be regulated. A too sudden decrease in intracerebral pressure is undesirable. When the fluid withdrawn is cloudy we always inject antimeningitis serum at once even though we suspect that some other organism may be the cause. The serum does no harm no matter what the organism may be, and if it is meningococcic meningitis the earlier serum is administered the better. Later treatment depends on the examination of the cerebrospinal fluid. We have used streptococcus and pneumococcus serums in appropriate cases. No patient with pneumococcus meningitis directly under our supervision has recovered, but we know of two patients who did. One patient with streptococcus meningitis out of fifteen recovered, but no influenzal patient. At present we have a good supply of anti-influenzal serum furnished us by Dr. Flexner, and as cases come along we shall use it.

As stated above, if the first fluid is cloudy we inject antimeningitis serum. It is warmed to body temperature and injected very slowly by gravity under the least possible pressure. This method was introduced by Koplik. A syringe is dangerous, and is probably responsible for many deaths following the administration of serum. In general, the dose for an adult is from 20 to 40 c.c., and for infants and children from 3 to 20 c.c. The amount depends as much on the quantity of cerebrospinal fluid withdrawn as on the age. An infant will frequently stand 20 c.c. without difficulty. The dose should usually be at least 5 or 10 c.c. less than the amount of cerebrospinal fluid withdrawn.

We have seen a number of cases of undoubted dry taps during the course of cases of meningococci meningitis. The serum ran in freely and showed the usual variation in movement depending on respiration. In such cases it is advisable to proceed very slowly and to watch the patient carefully for the slightest change in pulse and respiration. We think that possibly in some cases the exudative period is followed for a short time by one of decreased secretion. At any rate, a dry tap is frequently followed by one in which fluid is obtained. In cases with thick exudate that will not flow through the needle, gentle suction with a syringe may be tried. If that fails a little serum injected will sometimes start the flow. In very severe cases we inject the serum every twelve hours until there is improvement. In moderate and mild cases we usually repeat it each day for the first four days. Further administration depends on the patient's general condition and the bacteriologic examination of the fluid. Usually from 4 to 6 injections are necessary, but we have employed as many as sixteen or more. We consider that we get better results if the patient is turned from side to side so that no two successive punctures are done with the patient lying on the same side. That insures the emptying of the lateral ventricles in rotation.

A number of times during or immediately after the injection of serum the patient has gone into shock. Respiration has become slow and shallow or ceased, the facies pale and pinched and the pulse rapid and thready. At first this was very alarming, but we have never had a patient die from it. If the needle is still in place we withdraw some of the serum. Artificial respiration is resorted to if breathing has ceased and hypodermic stimulation is given for the heart. We have seen it happen much less frequently since we have been using smaller doses.

The serum we have been using lately contains 0.2 per cent. trikresol; earlier it contained 0.3 per cent. As is well known, the trikresol has been blamed by several physicians, especially Dr. Kramer of Cincinnati, for the fatal results that have been reported in a few instances following the injection of antine meningitis serum, usually in young children. Hale, of the Hygienic Laboratory at Washington, and Auer, of Rockefeller Institute, report experiments with dogs showing that serum containing trikresol is somewhat more toxic than unpreserved serum or that containing chloroform or ether. Auer carried on experiments with monkeys also, and showed that they were far less sensitive to trikresol serum than the dogs. Furthermore, in France, where serum without preservative is used, cases of shock and occasional fatal results are reported. As stated above, we have never seen such a case, although we have administered the serum considerably over five hundred times and to children of all ages, fourteen of our patients being under a year old. In view of our experience with serum that has always contained trikresol, we cannot believe that it is the cause of the fatalities. We think rather, that they may be due to injudicious administration of the serum — too large doses, or too rapid increase of pressure, which is likely to happen unless the gravity method is used — or to an unusual susceptibility on the part of the patient. On account of the fear of trikresol — unfounded, we feel — that has been produced by these reports, it seems advisable to try for a while the use of chloroform or a preservative. A comparison of the results with the serum prepared with the two different preservatives will enable us to decide which method is preferable.

We have not given the method of administering serum with the use of the blood-pressure apparatus a fair trial because we have so seldom had sufficient assistance to manage it. We think it is probably a help to those who have had little experience.

If a case shows a tendency to become chronic we make an autogenous vaccine and give it every four or five days in doses of from 250 to 1,000 million. Sometimes it has seemed to be very effective, but we have not had enough cases to be able to draw definite conclusions. We can say that we have never seen it do any harm. In treating cases it

must be remembered that frequently the stiff neck is the last symptom to disappear and if the fluid has cleared up and the temperature stays down it may be entirely disregarded.

The use of hexamethylenamin (urotropin) comes between general and specific treatment. We recommend its administration in all acute meningeal infections. It is said that twenty minutes after its administration formaldehyd can be detected in the spinal fluid. It may not be there in sufficient amounts to do much good, but the procedure seems rational. The fact that meningococci may be isolated from the urine is another argument for its use. In one case of *Streptococcus mucosus capsulatus* meningitis we gave hexamethylenamin dissolved in normal saline intraspinally. The temperature dropped from 106 F. to 102 F., and the patient became rational, but the case terminated fatally.

In planning the general treatment we find it necessary to remember that epidemic cerebrospinal meningitis may be a greatly prolonged febrile disease. The patient is best kept in a quiet darkened room. Sedatives are needed if the patient is very restless. We have had one fatal prolonged case in which we thought the patient might have been saved had the doctor given her an opiate so that she might occasionally have had a few hours of rest. The bowels and bladder should receive careful attention, particularly the bladder. Retention and cystitis are not uncommon. The patient should be examined for a distended bladder daily and the family warned to report infrequency of micturition. Patients should not lie in a draught and should be carefully covered up, especially during and after puncture. We have learned by bitter experience how easily they fall victims to pneumonia. In ordering the hygiene of the sick-room it must be remembered that the meningococci are found in the secretions of the nose and throat and in the urine. The diet should be such that it may be easily digested but generous in amount. The high caloric diet of typhoid is indicated for the reason that meningitis-like typhoid may be prolonged. The ice-bag gives a measure of relief for the headache.

Among the complications we have had:

| | |
|-------------------------------|---------|
| Pneumonia in | 7 cases |
| Basic meningitis in | 6 cases |
| Paralysis in | 3 cases |
| Hydrocephalus in | 3 cases |
| Deafness in | 3 cases |
| Cystitis in | 2 cases |
| Serum rash in | 2 cases |
| Iritis in | 2 cases |
| Typhoid in | 1 case |
| Scarlet fever in..... | 1 case |
| Measles in | 1 case |
| Purulent otitis media in..... | 1 case |
| Blindness in | 1 case |
| Arthritis in | 1 case |

In no case of basic meningitis under our care has recovery ever ensued. At first we used to try very hard to get the patients into hospitals to have brain puncture done. Now we explain to the family that it may do some good, but do not urge it strongly because we do not feel that it is of much avail. Of the cases with paralyses, two cleared up. One case of deafness cleared up entirely after the lapse of several months. The patients with typhoid and measles both recovered. We are much interested in the question of mental deterioration following meningitis and are following up our cured patients. In the course of time we shall have sufficient data from which to draw conclusions.

Table 5 shows our mortality statistics for the four years from July 1, 1910 to July 1, 1914.

TABLE 5.—MORTALITY, JULY 1, 1910, TO JULY 1, 1914

| Year | Total No. Cases | Patients Recovered | Patients Died | Result Unknown | Mortality Per Cent. |
|-----------|-----------------|--------------------|---------------|----------------|---------------------|
| 1910-1911 | 17 | 10 | 7 | 0 | 41 |
| 1911-1912 | 25 | 7 | 15 | 3 | 60 |
| 1912-1913 | 29 | 17 | 12 | 0 | 41 |
| 1913-1914 | 41 | 30 | 11 | 0 | 26 |

The 1911-1912 statistics need some explanation: four cases developed into basic meningitis and in five other fatal cases the patients were either in hospitals already or were sent there and we had slight oversight of the treatment.

We feel that this particular department — meningitis — is a worthwhile venture in treating cases of meningitis, in teaching physicians whom we see in consultation to administer serum and in training a group of experts who will be able to handle efficiently the outbreaks of meningitis that occur about every ten years in New York City.

THE LANGE GOLD CHLORID REACTION ON THE CEREBROSPINAL FLUID OF INFANTS AND YOUNG CHILDREN *

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This paper contains the results of the Lange reaction on the spinal fluids of some sixty odd children and infants. We are reporting these because of the evidence that the colloidal gold reaction is of undoubted value as an aid in the early diagnosis of many cerebrospinal diseases occurring in such patients.

The first work on colloidal gold was that done by Michael Faraday¹ in 1857. His colloidal solutions were made by reducing gold chlorid with phosphorus. It was not, however, until 1898 that Zsigmondy² devised the present-day method for making clear solutions or suspensions of colloidal gold. He gives several methods for making these gold hydrosols. The first method is the one used in making the indicator for our tests. Briefly, a dilute solution of gold is mixed with potassium carbonate and reduced at the boiling-point by formaldehyd.³ If clear red solutions are desired, which can be used as colloidal reagents, then the details as described in previous work must be followed.⁴ Zsigmondy further showed that on the addition of most electrolytes the red color quickly changes to a blue, and then deposits gold as an extremely fine powder.⁵ Another phenomenon discovered by him was that the presence of foreign colloids of certain kinds present the color change as well as the precipitation of gold. Even 0.0001 per cent. of gelatin is enough to do this. This phenomenon he designates *Goldschutz*, which for each albuminous body is quantitatively different. Each albuminous body, then, has a definite gold figure (*Goldzahl*) reckoned in terms of the number of milligrams necessary to protect 5 c.c. of goldsol against precipitation by 0.5 cm. of 10 per cent. sodium chlorid.⁶ It was further noted that 1 c.c. of

* From the Children's Wards of the Cook County, Presbyterian and Provident Hospitals, and the Laboratories of the Presbyterian and St. Luke's Hospitals.

1. Faraday, Michael: Proc. Roy. Soc., 1857, viii, 356; Phil. Mag., 1857, iv, 13, 401.

2. Zsigmondy: Ann. d. Chem. (Liebig's), 1898, ccc, 30.

3. Zsigmondy and Alexander: Colloids and the Ultramicroscope, Chap. viii.

4. Sippy and Moody: Trans. Am. Phys., 1913, p. 720. Grulee and Moody: Jour. Am. Med. Assn., 1913, lxi, 13.

5. Zsigmondy and Alexander, Chap. iii, p. 78.

6. Zsigmondy and Alexander, Chap. iii, p. 79.

0.4 per cent. sodium chlorid would have no effect on colloidal gold. Then, if one diluted the serum in 0.4 per cent. sodium chlorid a point would be reached at about 1:1,500 which is the optimum dilution of globulin to precipitate out the goldsol, whereas, if this dilution is made with distilled water there is no optimum dilution point.

With this as a basis Carl Lange⁷ in Wechsellmann's laboratory in Berlin set out to apply the principle in testing pathologic spinal fluids. At that time he was interested primarily in the spinal fluids of syphilitics whom Wechsellmann was treating by the salvarsan method. The technic as worked out by Lange is briefly as follows:

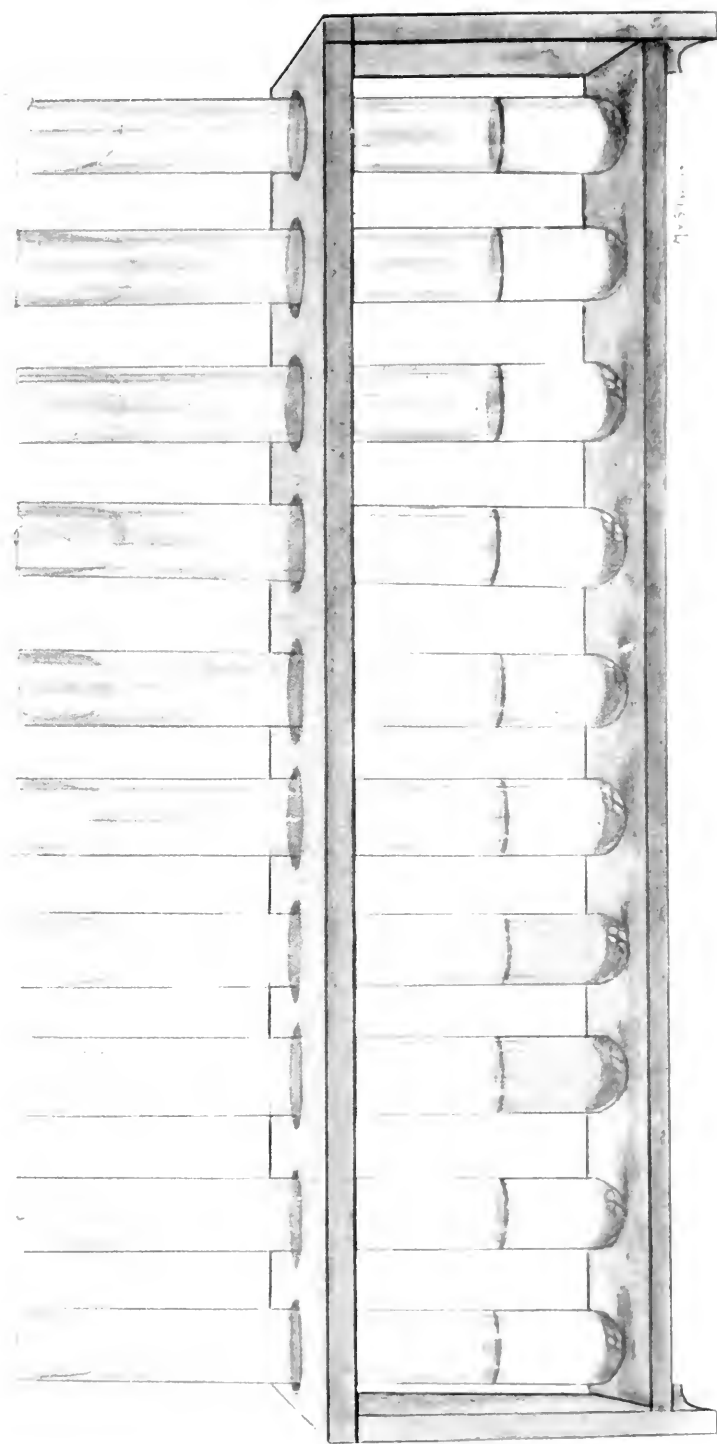
TECHNIC OF GOLD CHLORID REACTION

A series of test-tubes (6 by $\frac{3}{4}$ in size) is used. In the first tube place 1.8 c.c. of a 0.4 per cent. sodium chlorid solution (freshly made from a stock 10 per cent. solution), and 1 c.c. in each of the succeeding nine. Then take 0.2 c.c. of the spinal fluid to be tested and add to the first tube, thus making a dilution of 1:10. This is mixed with a 1 c.c. pipet. One c.c. is removed and added to a second tube, making a dilution in this tube of 1:20. This procedure is carried on throughout the series, the remaining quantity being thrown away. When the dilutions are finished there is 1 c.c. in each tube, and the dilutions vary from 1:10, 1:20, 1:40, 1:80, etc., up to 1:5,120 in the last tube. Then add rapidly to each tube 5 c.c. of the indicator, which is a colloidal solution of gold.

As stated above, it is the making of the indicator that requires the greatest amount of care, because there are many small but important factors necessary to observe absolutely in order to obtain a useful indicator. Briefly, we may say that absolute chemical cleanliness and the following of the technic in detail as it is described is the only possible way to obtain the best indicator. A good indicator is necessary for accurate results from the test. The indicator when good is absolutely clear, is red in color, with some yellow and a tinge of purple. If kept in a clean Jena glass flask away from the light it will remain unchanged for months.

The tests when made should stand for twenty-four hours to get the maximum amount of reaction before taking a final reading. Nevertheless, one can within fifteen to thirty minutes, and in many cases sooner, tell what the result will be. This is especially true of any strong reaction. For convenience and to facilitate the reading and interpretation of the results obtained by the test in general, the reactions may be divided into three groups. The first group includes the reactions which are strongest in dilutions of 1:40 and 1:80 (third and fourth tubes). Second group, those having maximum reactions in the fourth, fifth and sixth (1:80, 1:160, 1:320) tubes; third group,

⁷ Lange, Carl: *Ztschr. f. Chem. u. verwandte Gebiete*, 1913, i, No. 1, pp. 44-78.



The usual reaction of the Lange gold chloride test on the cerebrospinal fluid in congenital syphilis



the reactions which are strongest in the seventh to tenth (1:640 to 1:5,120) tubes.

The diseases of the brain and cord falling into the first class are those due to syphilis, that is, syphilitic meningitis, gumma of the brain, tabes dorsalis, general paresis and congenital syphilis. In all of these the maximum reaction is in the third and fourth (dilutions 1:40 and 1:80) tubes. These involve certain variations which will be taken up later. Syphilitic meningitis, gumma of the brain, as well as congenital syphilis, give, as a rule, a red-blue or violet color. This would be designated as a 2 reaction. Tabes dorsalis early in the disease or after treatment might give the same type of reaction. In a well-developed tabes, however, there is usually a 3:5 (dark to light blue or water white) reaction at 1:40 and 1:80 with the reaction fading gradually to the left and rather abruptly to the right. General paresis gives, even early in the disease, a reaction typical for that condition alone. So constant is the reaction that one may venture a diagnosis without other findings either clinical or laboratory. This reaction is the strongest of them all and in it we see an absolutely clear, colorless fluid (5) in the first four, five or even as high as the eighth tube, with a (2) reaction in the tenth tube. A taboparetic spinal fluid early would react strongly—approaching very closely the reactions for a true general paresis.

The reactions in the second group are rarely stronger than a dark blue (3) and usually lie between a red-blue and a violet (2 to 3). Tuberculous meningitis usually gives the strongest reactions of any of this group. The point of maximum reaction is usually in the fifth and sixth (dilutions 1:160 and 1:320) tubes. As the disease progresses it may approach the higher dilutions. In two cases of this series in which the spinal fluid was tested shortly before death occurred, the maximum reaction was in the eighth tube (1:1,280). In this respect it resembles the reaction occurring in suppurative meningitis. Brain tumors, toxic meningitis (meningismus), edemas from sunstroke, uremia, etc., may give a slight reaction of equal intensity in the fourth, fifth and sixth tubes (1:80, 1:160 and 1:1,320) when they react at all. Brain tumors in the presence of normal spinal fluid give no reaction.

All stages of acute encephalitis on to brain abscess belong also in this second group. The reaction approaches more nearly that for syphilis than any other type of lesion. The maximum reaction is usually in dilutions of 1:80 and 1:160, but extending toward the higher dilutions, thus differing from syphilis.

Suppurative meningitis from any cause will give a strong reaction in the higher dilutions, usually strongest in the seventh and eighth

tubes (1:60⁸ and 1:1,200). This is usually a dark blue color (3), but may be so strong that a clear, colorless (5) reaction will occur.

Group colloidal gold reactions for syphilis and tuberculous meningitis have been reported more recently by Eicke⁸ and Lee and Hinton.⁹

Miller and Levy¹⁰ conclude that the Lange reaction "is of no aid in the diagnosis of purulent or tuberculous meningitis," and that "it has no advantage over known laboratory procedures in the diagnosis of congenital syphilis." After reading the results recorded in their paper, we do not believe that they have drawn proper conclusions. They report 100 per cent. positive Wassermann reactions in congenital syphilis cases, however. We have been unable to get such results.

The following precautions were taken in obtaining the cerebrospinal fluid: After sterilization of the puncture needle it was thoroughly cleansed with alcohol and then with ether; the skin was washed with iodine and the iodine removed with alcohol. All fluids were rejected in which blood could be recognized. The Wassermann reaction, when tested, was made on the cerebrospinal fluid, unless otherwise mentioned in the tables. We might state that we were strongly impressed by the fact that in congenital syphilis a rather florid state of the disease is required to produce a positive Wassermann reaction.

Table 1 is a report of eighteen cases of congenital syphilis. It will be seen that in every one of these cases there was a definite precipitation in the gold chlorid solution. This reaction in every case showed its greatest intensity in the dilutions of 1:40 and 1:80. In only one instance, Case 14, was there any reaction above the dilution of 1:320. In Case 3 and Case 9, after, respectively, seven weeks and one year of treatment, the reaction was materially altered, in Case 3 no reaction appearing, and in Case 9 the reaction being very markedly reduced.

Table 2 contains reactions of four infants. These reactions are peculiarly similar to those obtained in parietic dementia in adults. It is for that reason that they have been separated from the cases tabulated in Table 1.

It will be noted that in all these cases in the first six dilutions the precipitate was great, and that in the first case the precipitate was almost complete throughout. In Cases 1, 2 and 3 death occurred in from five days to two months after the examination of the cerebrospinal fluid, but unfortunately in none of these cases could a necropsy be obtained.

⁸ Eicke. *München. Med. Wehnschr.*, 1913, ix, 2713-2717.

⁹ Lee and Hinton: *Ann. Jour. Med. Sc.*, 1914, cxlviii, 33.

¹⁰ Miller and Levy: *Bull. Johns Hopkins Hospital*, 1914, xxv, No. 279, 133.

TABLE 1.—CONGENITAL SYPHILIS

| Name | Age | Nonne | Cell- Count | Wass- ermann | Lange Gold Chlorid Dilutions | | | | | | | | Remarks | | |
|----------------------|---------|-------|----------------|-----------------|------------------------------|------|------|------|-------|-------|-------|--------|---------|--------|---------------------------|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1280 | | 1/2560 | 1/5120 |
| 1. Harold G. | 3 wks. | + | .. | — | 2 | 2 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | After 7 weeks' treatment. |
| 2. Helen W. | 6 wks. | ± | .. | — | 2 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | |
| 3. Anna K. | 13 wks. | + | .. | — | 2 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | |
| 4. James McK. | 2 mos. | — | .. | — | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 5. Vincent W. | 2 mos. | — | .. | — | 1 | 1 | 2 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | |
| 6. Louisa W. | 3 mos. | — | .. | — | 2 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | After 1 year's treatment. |
| 7. Baby M. | 4½ mos. | — | .. | + | 3 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | |
| 8. Louise C. | 5 mos. | — | .. | — | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 9. Baby C. | 6 mos. | + | .. | — | 3 | 4 | 5 | 4 | 2 | 1 | 0 | 0 | 0 | 0 | |
| 10. Ruth S. | 6½ mos. | — | .. | — | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 11. Baby Ma. | 7 mos. | — | .. | + | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 12. Mary M. | 9 mos. | — | .. | — | 2 | 3 | 3 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | |
| 13. Gertrude R. | 10 mos. | ± | .. | — | 1 | 2 | 3 | 3 | 3 | 1 | 1 | 0 | 0 | 0 | |
| 14. Joe C. | 11 mos. | ? | .. | — | 1 | 1 | 3 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | |
| 15. Armando M. | 1 yr. | — | .. | — | 2 | 3 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | |
| 16. Nick L. | 1 yr. | — | .. | — | 1 | 1 | 3 | 3 | 3 | 3 | 1 | 0 | 0 | 0 | |
| 17. Olga A. | 2½ yrs. | — | .. | + | 2 | 3 | 4 | 4 | 3 | 3 | 1 | 0 | 0 | 0 | |
| 18. Baby E. | 4 yrs. | + | .. | — | 2 | 3 | 5 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | |

TABLE 2.—REACTION LIKE THAT OF PARETIC DEMENTIA

| Name | Age | Nonne | Cell- Count | Wass- ermann | Lange Gold Chlorid Dilutions | | | | | | | | | | Remarks |
|----------------|---------|-------|----------------|-----------------|------------------------------|------|------|------|-------|-------|-------|---------|---------|---------|-------------------------------------|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1,280 | 1/2,560 | 1/5,120 | |
| 1. Eva R. | 7 mos. | ++ | ++ | .. | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 4 | 4 | 1 | Death within 1 week. |
| 2. Thomas C. | 11 mos. | ++ | 20 | + | 5 | 5 | 5 | 5 | 4 | 3 | 2 | 0 | 0 | 0 | Death in 5 days. |
| 3. Dorothy H. | 13 mos. | ++ | 70 | .. | 5 | 5 | 5 | 4 | 4 | 1 | 0 | 0 | 0 | 0 | Death in 2 months. |
| 4. Florence R. | 5 yrs. | ++ | 70 | + | 5 | 5 | 5 | 5 | 4 | 3 | 2 | 1 | 0 | 0 | Many symptoms of parietic dementia. |

Patient 4 was a little girl of 8 years who entered the Presbyterian Hospital July 19, 1913, on the service of Dr. Bassoe. The history was as follows: Father and mother were well; three younger brothers, all healthy, normal and strong; there was one premature birth, the first child, with death three weeks after birth; after this a miscarriage at seven months; then the patient was born, and after her the three boys above mentioned. There is no family history of imbecility, idiocy, etc.; no history of tuberculosis or syphilis. The child had measles and mumps when a year old, but up to the fifth year she was apparently perfectly normal and then she began slowly to show signs of idiocy. This began by running over a lot of words which had no sense to them. She gradually developed incontinence of feces and urine. She recognized only her parents and brothers; she did not cry much, ate well and had no pain. She was nervous; her knees seemed weak; her right arm was weaker than the left and was slowly getting worse. She was easily frightened but slept soundly. On physical examination the pupils of the eyes were found large and reacted slowly to light; nose and ears negative; teeth irregular; thyroid was not to be palpated; there were no abnormal findings in the chest or abdomen. As to the extremities, it was noticed that the fingers of the right hand were somewhat overextended, especially in the end phalanges. Reflexes: Pupils reacted very slowly to light; the patellar reflex was exaggerated; Achilles and arm reflexes were present and there was some question as to the Babinsky. As to her speech, it was found that some of the common things she could say very well, and this would be followed by words which made no sense.

There is enough in this history to make one at least strongly suspicious of the presence of a paretic dementia, even though this condition is quite rare at this age.

As to the interpretation of the other three cases, it is impossible for us to offer any suggestions. It seems, however, that investigation of such cases is well worth future study.

Table 3 contains twelve cases which we were not able to show positively clinically were congenital syphilis. There was, however, in every case a strong suspicion. It will be noted in this series, too, that with the exception of Case 6, reaction was most marked in the dilutions of 1:40 and 1:80.

Patient 6, Grant R., entered the Presbyterian Hospital on the service of Dr. Grulee on May 27, 1914, aged 1 year. He came in with the complaint that the present trouble began with a cold in the head and croup six weeks before. During the previous week the condition had been getting much worse; breathing was difficult and wheezy. The child had never been cyanotic. The stools were green and contained curds, and there was no vomiting. The child had been breast-fed up to three or four days before entrance; had never been previously ill; there was very marked dyspnea on expiration and inspiration. The child cried seldom but its cry was hoarse. There was marked retraction of the lower end of the sternum; in the sternal region there was diminished resonance and flatness which extended one finger's breadth to the left of the sternum; over the whole chest breath sounds were loud and wheezy; bronchophony over the spine within one finger's breadth of the lowest level of the spine of the scapula; no fine râles.

In the abdomen the spleen was found to be two fingers' breadth below the ribs and was firm; the liver was not enlarged. The cervical axillary and inguinal glands were enlarged but no epitrochlears were felt. Examination of the larynx by Dr. Friedberg showed a subglottic swelling which was probably

TABLE 3.—SUSPECT CONGENITAL SYPHILIS

| Name | Age | Nonne | Cell-Count | Wass.-ernann | Lange Gold Chlorid Dilutions | | | | | | | | | | Remarks |
|---------------|---------|-------|------------|--------------|------------------------------|------|------|------|-------|-------|-------|---------|---------|---------|--|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1,280 | 1/2,560 | 1/5,120 | |
| 1. Helen C. | 6 wks. | ± | .. | .. | 1 | 2 | 4 | 5 | 4 | 1 | 0 | 0 | 0 | 0 | Also tetany. Severe anemia. Severe anemia. |
| 2. Irene N. | 3 mos. | + | .. | .. | 1 | 2 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 3. Vladimir | 5 mos. | + | .. | .. | 1 | 2 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 4. Peter L. | 9 mos. | + | .. | .. | 0 | 3 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 5. Forrest S. | 11 mos. | ± | .. | .. | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 6. Grant R. | 1 yr. | ± | 12 | — | 1 | 2 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 7. Walter R. | 15 mos. | — | .. | .. | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 8. Ethel F. | 18 mos. | + | .. | .. | 3 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 9. Nick N. | 2 yrs. | + | .. | + | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 10. Wyd. St. | 2½ yrs. | ± | .. | + | 3 | 3 | 5 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 11. Gladys | 3 yrs. | ± | .. | + | 2 | 3 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | |
| 12. Mart. B. | | — | .. | .. | 3 | 5 | 5 | 5 | 2 | 0 | 0 | 0 | 0 | 0 | |

TABLE 4.—TUBERCULOUS MENINGITIS

| Name | Age | Nonne | Cell-Count | Wass.ermann | Lange Gold Chlorid Dilutions | | | | | | | | | | Remarks |
|---------------------|---------|-------|------------|-------------|------------------------------|------|------|------|-------|-------|-------|---------|---------|---------|---------------------------------|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1,280 | 1/2,560 | 1/5,120 | |
| 1. Ralph B. | 2½ mos. | — | 71 | .. | 1 | 1 | 2 | 4 | 4 | 3 | 1 | 0 | 0 | 0 | Questionable; symptoms typical. |
| 2. Madeline R. | 4 mos. | ++ | .. | .. | 0 | 0 | 0 | 1 | 1 | 3 | 4 | 3 | 0 | 0 | |
| 3. Irene P. | 7 mos. | — | .. | .. | 0 | 0 | 0 | 0 | 2 | 3 | 4 | 4 | 2 | 0 | |
| 4. Harry K. | 18 mos. | ++ | 150 | — | 0 | 0 | 2 | 3 | 5 | 5 | 5 | 1 | 0 | 0 | |
| 5. Harold R. | 3 yrs. | ++ | .. | .. | 2 | 2 | 3 | 4 | 5 | 3 | 1 | 0 | 0 | 0 | |
| 6. Blanche G. | 3 yrs. | ++ | .. | .. | 3 | 3 | 3 | 4 | 5 | 5 | 5 | 1 | 0 | 0 | Syphilitic meningitis. |
| 7. Roy A. | 4½ yrs. | — | .. | .. | 1 | 1 | 2 | 3 | 4 | 4 | 2 | 1 | 0 | 0 | |
| 8. Charles S. | | + | 57 | + | 1 | 1 | 1 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | |

an edema. The blood showed 3,560,000 reds, 17,900 whites, and 50 per cent. hemoglobin (Dare).

The child rapidly improved on a powder consisting of mercury with chalk, $\frac{1}{2}$ grain, and sodium bromid, 2 grains, given three times a day. The child left the hospital on June 7 much improved, and from recent reports, on continuing the same treatment the improvement has been steady. The Roentgenogram showed a shadow in the mediastinum which appeared to be a mass of enlarged mediastinal glands. Whether this is a case of congenital syphilis or not, we do not feel competent to say.

Among these cases were two, Cases 5 and 11, in which a severe anemia was gradually but materially benefited by mercurial treatment.

SUMMARY

Summing up the gold chlorid reaction as it occurs in congenital syphilis, it seems to us that the following may be stated:

There are two types of reaction which occur in cases of congenital syphilis; one in which the height of the reaction is obtained in the dilutions of 1:40 and 1:80; in higher dilutions there is a distinct tendency to less reaction, and this reaction never continues past the dilutions of 1:640, and infrequently past the dilutions of 1:160. The second reaction approaches closely that of parietic dementia and needs further investigation before it can be properly interpreted.

Table 4 contains the reactions in eight cases of tuberculous meningitis. In five of these cases the reaction was most marked in the dilutions of 1:160 and 1:320. In two the reaction was greatest in dilutions of 1:640 and 1:1,280; in one at 1:40 and 1:80. In Case 2 the diagnosis of miliary tuberculosis with tuberculosis of the meninges was confirmed at necropsy.

The diagnosis of Case 1 is questionable, principally because of the age. No signs of general miliary tuberculosis were to be found. The case may have been one of syphilitic meningitis. The child left the hospital and it was impossible to trace it further. There is little question that there is marked reaction of the colloidal gold chlorid solution to the cerebrospinal fluid in tuberculous meningitis.

Very few conclusions may be drawn from such a small series of cases. In five of the eight cases the reactions were most marked in the dilutions of 1:160 and 1:320. It is a noticeable fact, however, that in two cases the reaction was most marked in the dilutions of 1:640 and 1:1,280, the same as in the case of septic meningitis, Table 5, Case 3. After examination of the cerebrospinal fluid in tuberculous meningitis in adults, we have come to look on the first-noted reaction as the more typical and almost never to expect reaction in dilutions of 1:640 and 1:1,280 except in cases of septic meningitis.

In Table 5 are included those cases in which there were symptoms of conditions affecting the mentality or meninges. In this have been

TABLE 5.—OTHER CEREBRAL CONDITIONS

| Name | Age | Nome | Cell-Count | Wassermann | Lange Gold Chlorid Dilutions | | | | | | | | Remarks | | |
|--------------------|---------|------|------------|------------|------------------------------|------|------|------|-------|-------|-------|---------|---------|---------|--|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1,280 | | 1/2,560 | 1/5,120 |
| 1. Benny T. | 2½ yrs. | + | 14,700 | .. | 0 | 1 | 2 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | Pneumococcus (?) meningitis. |
| 2. Charles N. | 1 yr. | ++ | .. | + | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | Pneum. Mening. (necropsy). |
| 3. Sarah R. | 3 mos. | +++ | .. | .. | 1 | 1 | 1 | 1 | 3 | 4 | 4 | 3 | 1 | 1 | Septic meningitis. |
| 4. Edwin B. | 21 mos. | + | .. | .. | 1 | 2 | 4 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | Meningismus Susp. of Syph. |
| 5. Dale H. | 7 yrs. | ? | .. | .. | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | Pneum. and meningismus. |
| 6. Homer B. | 9 yrs. | ? | 38 | — | 1 | 2 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | Meningismus (?). |
| 7. Jake P. | 5 yrs. | ? | 2 | .. | 1 | 2 | 3 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | Hydrocephalus. |
| 8. Michael M. | 5 yrs. | — | .. | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Cretinism. |
| 9. John Z. | 7 yrs. | .. | .. | .. | 0 | 0 | 1 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | Agenesis of brain with edema ex vacuo; no signs of syph. |
| 10. Marie B. | 8 mos. | + | .. | + | 2 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | Idiocy following encephalitis. |
| 11. Tony R. | 6 yrs. | .. | .. | .. | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |

TABLE 6.—OTHER CONDITIONS

| Name | Age | Source | Cell-Count | Wassermann | Lange Gold Chlorid Dilutions | | | | | | | | | | Remarks |
|---------------------|---------|--------|------------|------------|------------------------------|------|------|------|-------|-------|-------|---------|---------|---------|---|
| | | | | | 1/10 | 1/20 | 1/40 | 1/80 | 1/160 | 1/320 | 1/640 | 1/1,280 | 1/2,560 | 1/5,120 | |
| 1. Edmund D. | 2 yrs. | .. | .. | — | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Pneumonia. |
| 2. Charles S. | 9 mos. | 0 | .. | .. | 2 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Leban pneumonia. |
| 3. John C. | 23 mos. | .. | .. | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Intoxication. |
| 4. Frank D. | 10 mos. | .. | .. | .. | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Intoxication. |
| 5. Theodore H. | 16 mos. | .. | .. | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Absolutely no signs of syphilis; decomposition. |
| 6. Thomas C. | 3 mos. | .. | .. | .. | 1 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | becomp. and otitis media. |
| 7. Tina M. | 9 mos. | .. | .. | — | 4 | 4 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | becomp. and acute nephritis. |
| 8. Katrina K. | 2½ mos. | .. | .. | .. | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | Pylorospasm. |
| 9. Infant A. | 5 mos. | .. | .. | .. | 1 | 2 | 3 | 3 | 2 | 1 | 0 | 0 | 0 | 0 | Prematurity. |
| 10. Vladimir | 6 mos. | ? | .. | .. | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | Miliary tuberculosis. |
| 11. Anna R. | 1 yr. | + | 2 | + | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | Tumor of the parotid. |

* Negative in spinal fluid, positive in blood.

included two cases of cretinism. In Cases 1, 4, 5, 6, 7 and 10, the reaction is seen to be similar to that of congenital syphilis. Case 1 was a case of meningitis due to diplococci, probably pneumococci. Case 4 was a case of meningismus in which there were strong suspicions of congenital syphilis. Cases 5 and 6 were also cases of meningismus but in neither of these cases was there any reason to suspect syphilis. Case 7 was a case of chronic hydrocephalus, probably of congenital origin. Case 10 was a case of idiocy in which the Wassermann and gold chlorid tests were both positive for syphilis, but which at necropsy showed nothing anatomically which would bear out this diagnosis.

The difference in the reactions of the cerebrospinal fluid in the two cases of cretinism is worthy of notice. Case 9 was far more advanced than Case 8. Whether this accounts for the greater reaction, it is impossible to say.

It is to be noted that in Case 2, while the Nonne and Wassermann were distinctly positive, the reaction to the gold chlorid was slight.

Table 6 contains eleven cases in most of which the patients were examined to obtain fluids which could be used as controls. It will be noted that four of these showed reactions which corresponded to the reactions of congenital syphilis. Of these, one, Case 11, gave at the same time a positive Wassermann reaction. Patient 9 was a premature baby and some suspicions of syphilis may attach to it. Case 10 was a case of miliary tuberculosis with distinct signs of involvement of the meninges. Case 7 was one of severe marasmus in a Greek baby 9 months old. The child had no certain enlargement of the spleen; there was, however, a mass in the left upper abdominal region which might have been an enlarged spleen. The epitrochlear glands were enlarged in addition to this, and the child showed marked involvement of the kidney which was rather in the nature of a severe pyelocystitis than of a nephritis. There were some points in this which might suggest the possibility of a congenital syphilis; at least its presence cannot be absolutely ruled out.

It should be stated that the amount of cerebrospinal fluid obtained was in many instances too small for use in making the cell count and Wassermann reaction after the Nonne and gold test had been made

CONCLUSIONS

1. In the cases of congenital syphilis included in this report the cerebrospinal fluid reacted to the colloidal gold chlorid solution always in the lower dilutions, and with a marked degree of regularity strongest in the dilutions of 1:40 and 1:80.

2. There is a small group of cases of congenital syphilis in which the reaction is similar to that of parietic dementia.

3. The reaction as obtained in congenital syphilis is most nearly approached by those conditions which show a slight inflammation of the meninges or brain and are not likely to be confused clinically with syphilis.

4. The reaction in tuberculous meningitis is found to be most intense in the dilutions of 1:160 and 1:320. It is likely that the more rapid the course the more apt is the reaction to occur in the higher dilutions.

5. From the foregoing statistics it is evident that the Lange gold chlorid reaction is of value only as an aid in diagnosis.

In addition to the references in the preceding text the following may be referred to:

Kaplan, D. M., and McClellan, J. E.: *Jour. Am. Med. Assn.*, 1914, lxii, 511
DeCrisis, Max, and Eberhardt, Frank: *München. med. Wchnschr.*, 1914 xxii, 1216.

Smith, L. D.: *Illinois Med. Jour.*, 1914, xxvi, 420.

Brock, G. W.: *Illinois Med. Jour.*, 1914, xxvi, 422.

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ACIDOSIS WITH AUTO-INTOXICATION IN INFANTS AND CHILDREN

A STUDY OF ONE HUNDRED CONSECUTIVE CASES IN APPARENT
EPIDEMIC FORM *

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CONCORD, N. H.

Between Nov. 18, 1913, and Feb. 1, 1914, in Concord, N. H., and its immediate neighborhood, there were approximately two hundred cases of illness associated with the presence of acetone bodies in the urine. They were diagnosed as cases of acidosis, and while some were doubtless of an inconsequential type that would ordinarily have escaped detection, the majority showed definite symptoms of severe auto-intoxication—symptoms wholly out of proportion to any obvious organic cause. Sporadic cases of acidosis in children, with auto-intoxication and recurrent vomiting, are not rare in that city; but it appeared that in this instance we had to deal with the disease in epidemic form. There were nine fatalities.

I have tabulated 102 consecutive cases, two of which were in women, aged, respectively, 38 and 36. If we eliminate these women we are left with an even hundred cases in infants and children. In the two adults the histories and symptoms were quite analogous to those portrayed in the larger group.

But three infants out of a hundred were less than a year old. Eight were between 1 and 2 years. The great bulk of the patients—eighty in all—were fairly evenly distributed among the ages from 2 to 8. Then came a few scattering cases up to 13, the age of the oldest child. There were 59 boys and 41 girls—a deviation from the accepted ratio.

In view of the fact that Concord is a well-to-do city with comfortable homes, one would expect that the majority of the afflicted children would be well nurtured. Twenty of the homes I have listed as fair, the remainder as good or excellent. None were distinctly poor. Either tenements were notably exempt or else their quota escaped detection.

The earliest cases were discovered at Penacook, five miles from Concord, the middle of November. On December 1 a case was reported

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at Boscawen, 10 miles distant, and later in the month children were taken ill at Canterbury, 10 miles away in another direction. The first case to be diagnosed in Concord itself occurred on December 1. The fact that a wide territory was involved has a distinct bearing on water and milk as causative factors, for both of these were procured from a variety of sources. In Concord, the city water analyzed exceptionally well; milk came from at least a dozen dealers. In the surrounding towns both milk and water came, as a rule, from the farms on which the patients lived. Two infants were on breast-milk with crackers added; one had had nothing but breast-milk for three weeks preceding onset — a point at variance with Schrack's opinion (see Morse¹) that the acetone bodies are not excreted with a pure milk diet. There is evidence that no frozen milk had been used and that no unusual food, such as ensilage, had been given to the cattle.

A few children had eaten unwisely just before the onset of symptoms. One child of 6, for example, went to a party the day before her symptoms began. One of 3 was taken ill four days after eating a large Thanksgiving dinner. One of 5 ate canned shrimp the day before his illness began. One of 3 had pork pie two days before, while in a girl of 5 the parents attributed the attack to mince pie. These indiscretions lose their significance, however, when we find that in nine-tenths of the cases there had been no modification of diet previous to onset.

In only two instances was there evidence of abnormal fat consumption; while, on the contrary, several children were affected who, in order to prevent acidosis, had been most carefully fed on a carbohydrate diet. Thus a boy of 3 was taken ill who, for five days, had eaten only bread, gruels, toast, potato and milk. A boy of 7 for a week had had no solid food and no fats — simply gruels, broths and milk. A girl of 3, on account of a preceding tonsillitis, had been on a liquid diet with low fats and low proteids.

It seems probable that we cannot attribute so extensive an epidemic, if one may use the term, to the milk- or water-supplies, to starvation, to undue fat intake, or to any other dietary error.

The statement that a neurotic temperament plays a prominent part in the etiology of acidosis received scant substantiation. Not more than a fourth of the children were neurotic. In twenty-one the presence of adenoids was noted. Six children had both adenoids and enlarged tonsils, a point worthy of mention because we have found that the removal of adenoids and tonsils, in the intermittent type of acidosis, may be coincident with recovery.

In three instances the illness was ushered in by a bronchial asthma, beginning about twelve hours before the symptoms of intoxication

1. Morse: *Arch. Pediat.*, 1905, xxii, 561.

Four children had follicular tonsillitis immediately preceding. Two had pneumonia, but both pneumonias came late — afterwards as it were; and in several cases complicated with otitis media the same sequence was observed. Sixty-four children had either a coryza, a bronchitis or both. Occasionally, these two infections were concurrent with the acidosis; more often the infections preceded by three, four, five days or even a week. All told, then, in about 70 per cent. of these cases there was a well-defined infection of the respiratory tract or of its adjacent cavities. If we except one acute nephritis developing ten days after onset, no other types of infection were noted — no instances of complicating appendicitis, for example. In the remaining 30 per cent. — and this group includes two fatal cases — I can put my finger on no suggestive etiologic point.

Many of our patients were too young to attend school; some had apparently come in contact with no other children before they were taken ill. On various occasions two or more children in one house were sick at the same time; but, on the other hand, children were exempted who had been in intimate contact with affected children.

The epidemic was one of first attacks; eighty-four patients were ill of acidosis for the first time. Eleven cases were recurrent. One child had had as many as twenty attacks in eight years. We found that these recurrent attacks were more easily relieved than initial ones, as though a child, in time, acquired a low-grade immunity.

Almost invariably — eighty-six times — the onset was sudden. Prodromal symptoms were the symptoms of a preceding cold or coryza or none at all. Such premonitory derangements as anorexia, listlessness, headache and dizziness were unusual. Three times diarrhea preceded vomiting. Four times the two came together; but as a rule, vomiting came first and was the symptom denoting that a child was ill.

The commoner signs and symptoms enumerated in the text-books, with the number of cases out of a hundred in which they were observed, may well be tabulated:

| Signs and Symptoms | No. Cases |
|------------------------------|-----------|
| Coated tongue | 92 |
| Flushed face | 74 |
| Drowsiness | 64 |
| Thirst | 79 |
| Marked prostration | 41 |
| Wasting | 26 |
| Cerebral symptoms | 18 |
| Nervousness or activity..... | 22 |
| Air-hunger | 25 |
| Cyanosis | 16 |
| Mouth pallor | 23 |
| Retracted abdomen | 6 |
| Enlarged liver | 3 |
| Clay-colored stools | 7 |
| Icterus | 4 |
| Diarrhea | 35 |

The disease was seen in all degrees of severity. Mild cases yielded very quickly to treatment. Severe cases were pernicious in their activity. Fatal cases were malignant. The average duration of the fatal cases was thirty-two hours, the two extremes being sixteen hours in a baby 14 months old and sixty hours in a child of 5 years.

The more severe the attack the greater was the prostration and wasting, the more evident the meningeal symptoms. So great was the loss of fat in fatal cases that children, in a relatively few hours, shriveled from plumpness to emaciation. With sunken eyes, hollow cheeks and tight-drawn skin they looked not unlike patients in the late stages of phthisis. In such crises delirium and convulsions were expected; twice the clinical picture suggested meningitis.

A coated tongue, a flushed face, drowsiness and thirst were frequent during the active stage of illness. The type of air-hunger peculiar to the disease occurred without cyanosis, but cyanosis did not occur without air-hunger. Rarely a child's face showed complete pallor. Mouth pallor did not occur unless the face was flushed, but, on the other hand, many flushed faces showed no mouth pallor. Retraction of the abdomen was observed only in the more severe and protracted cases, no more frequently, as Griffith² says, than would occur in any asthenic state with empty intestines. Abdominal pain was infrequent, as was enlargement of the liver. Icterus, with clay-colored stools, was not nearly so common as other accounts would lead one to anticipate. One child exhibited a punctate red rash on the second day of disease. Otherwise skin lesions and pruritus (noted by Marcy³) were lacking.

In few more than a third of these cases was diarrhea observed. Here we had, characteristically, frequent, watery movements, barely colored, containing mucus and occasional fecal particles. A few stools were dark green, two or three were dark chocolate. Blood was almost never present. Normal or constipated stools, which prevailed in two-thirds of the cases, were brown, yellow or black. Watery stools had little odor; those that were solid or semi-solid were usually foul, and in all but one case in which the reaction was tested it was strongly acid. I cannot verify the statement that such stools show an excess of indican (Howland and Richards⁴).

In seven cases vomiting was absent. Normally, it was a predominant feature; food first, changing quickly to watery, mucous fluid, either colorless or yellow, like thin pea-soup. Vomiting was propul-

2. Griffith: *Am. Jour. Med. Sc.*, 1900, cxx, 553.

3. Marcy: *Internat. Clin.*, 1900, iii, 127.

4. Howland and Richards: *Arch. Pediat.*, 1907, xxiv, 401.

sive, frequent and copious. Blood was never present in the vomitus, but in eight instances there were considerable amounts of bile.

Temperature charts showed wide variations. Sixty-five patients exceeded 100 F., and temperatures of 103 or 104 were not uncommon; 105 was reached but once. Generally speaking, high temperatures were observed when there was delirium and marked prostration. On the other hand, of the fatal cases three ranged about 101, one about 100 and one about 99.4. Even subnormal temperatures were not unheard-of. The pulse was invariably elevated, averaging, with a low temperature, from 100 to 120. In children with high temperatures the rate ran as high as 160. There was no evidence of irregularity in the pulse—which heretofore has been described as a common symptom.

Another favorite phrase in the literature is "scanty turbid urine of high specific gravity." In this series we found:

| | |
|--|------------------|
| Clear urine | 91 |
| Turbid urine | 9 |
| Amount scanty | 50 |
| Albumin | 0 |
| Sugar | 1 (for two days) |
| Specific gravity (recorded in twenty-seven cases): | |
| 1.010 to 1.015..... | 4 |
| 1.015 to 1.020..... | 4 |
| 1.020 to 1.025..... | 10 |
| 1.025 to 1.030..... | 7 |
| Above 1.030 | 2 |
| Reaction invariably acid. | |

Considerable amounts of acetone were present in the urine in every case. Although exceptionally acetone did not appear in the urine until several hours after onset, in ninety-two cases it was found at the first test—practically at the beginning of acute symptoms—which leads to the belief that acidosis of this type is not a sequel of the persistent vomiting and starvation. Acetonuria almost never ceased while a urine was still acid; it tended, rather, to persist for several days after a urine became alkaline, especially if the diet was scanty, but in such an event a patient showed no toxic symptoms. During this period, however, if the urine was allowed to revert into its former acid condition, toxic symptoms were apt to recur. Acetonuria was of little moment, then, if one could procure alkalinity of the urine.

In examining for acetone, we used, commonly, the somewhat inaccurate nitroprussid test. The Lieben method seemed more delicate, while Rothera's test⁵ is said to act in a dilution of 1 to 130,000 (Piper⁶). Folin⁷ has stated that a large amount of acetone can be present in urine without giving a reaction (Piper⁶). A fruity odor in the breath, attributed to acetone, was noticed in a fourth of the cases. In several

6. Piper: *Lancet*, London, 1913, ii, 535.

5. Rothera: *Australian Med. Jour.*, October, 1910.

7. Folin: *Jour. Am. Med. Assn.*, 1907, xlix, 128.

analyses acetone was isolated in the stools and vomitus but only in minute traces.

In only forty-five individuals was the test for diacetic acid made. Fifteen of these were positive with ferric chlorid, but I believe that others would have yielded a positive reaction had specimens been tested more frequently and immediately after they were passed. We found:

Two fatal cases negative.

Three fatal cases positive.

Nine severe cases positive.

Three moderately severe cases positive.

The appearance of diacetic acid presumably indicated failing powers of oxidation. In an acid urine diacetic acid was a danger signal, and as recovery progressed it disappeared from the urine before acetone did.

Oxybutyric acid was found but once. A single analysis for nitrogen and ammonia gave: nitrogen, 10 gm.; ammonia, 0.33 gm.—quantities not far from normal. This child had, however, been under alkaline treatment, which would tend to decrease the absolute and relative excretion of ammonia (Beddard⁸).

We are told in the literature that recovery from acidosis with auto-intoxication is very rapid—as rapid as is the onset. This proved true in sixty cases. If we add our nine deaths we still have an appreciable number of patients that recovered slowly, requiring several days. One child died during this convalescence, apparently from exhaustion.

In this series, treatment comprised the administration of alkalis by mouth or by rectum, catharsis, rectal irrigations and the regulation of diet. Eighty-nine children were given sodium bicarbonate by mouth. Eighty successfully retained it. Three could not retain it; three retained it in part; three refused the solution. Soda was retained well in all but one of the fatal cases, although persistence of vomiting was expected until several doses had been given. The stomach proved tolerant of large amounts of soda.

Certain children preferred the dry salt; they deposited a teaspoonful on the tongue and washed it down with a swallow of water. Nevertheless, concentrated solutions tended to irritate the stomach and cause a recurrence of vomiting; and by concentrated solution I mean one stronger than 1:20; a dram of soda to $2\frac{1}{2}$ ounces of water. This ratio and the ratios 1:32 and 1:60 never caused nausea. Children who received a dram of the salt each hour or two acquired an alkaline urine in from twenty-four to thirty-six hours; those who received a

8. Beddard: Clin. Jour., 1912-13, xl, 65.

dram every four hours, in divided doses, acquired alkalinity in from forty-eight to sixty hours.

Irrespective of age, then, if soda is used, I believe that it is proper to make a solution in the ratio of 1:20. Of this solution half an ounce may be given every twenty minutes. No definite rule will fit every case, of course. One must often vary the dilution and the frequency of administration, but he should give the drug freely and in as concentrated a form as is well borne. Edsall's⁹ minimum dosage — 100 grains of the bicarbonate — given as rapidly as possible, is much less than was used for many of our cases. The same may be said of Rachford's¹⁰ suggestion that 8 or 10 grains be given every two or three hours and of Koplik's small dosage.¹¹

In fatal cases the progress of the disease was so rapid that it seemed impossible to give sufficient alkali — perhaps because "the alkalies are not of much value unless the supply of base to neutralize the acids has failed. If the cause is toxic . . . alkalies are unlikely to do good" (Cautley¹²).

Water proved the most satisfactory solvent for soda. Attempts to disguise the flavor of the salt with orange-juice or grape-juice were usually unnecessary. Of the two, orange-juice was preferable.

Sodium bicarbonate was given by rectum in thirty-two instances: half a dram of the salt in 2 ounces of water injected every hour or two. It was retained in eighteen. A saturated solution given by the drop method at the rate of a drop per second could be continued from twelve to twenty-four hours. It was useless to employ either method if a child had diarrhea.

Potassium citrate and sodium citrate were the alkalies of second choice, used both in conjunction with the bicarbonate and alone, either throughout the illness or during convalescence. One or the other citrate was given to fifty-two children. The citrates proved quite as palatable as the bicarbonate of sodium and were effective in procuring alkalinity. Some children could retain them who could not retain the bicarbonate; the reverse was occasionally true.

Citrates may be given to the amount of half a dram or a dram every hour, in a concentrated solution: 1 ounce of salt to 4 of water. So given, one procures an alkaline urine in less than twenty-four hours, and with these drugs alone one may conquer an acidosis with auto-

9. Edsall: *Brit. Med. Jour.*, 1910, ii, 1033; *Am. Jour. Med. Sc.*, 1903, cxxv, 629.

10. Rachford: *Diseases of Children*, New York, 1912, pp. 251 and 565.

11. Koplik: *Diseases of Infancy and Childhood*, New York, 1910, pp. 33 and 505.

12. Cautley: *The Diseases of Infants and Children*, London, 1910, 149.

intoxication. The administration of any alkali should be continued for a few days after the subsidence of acute symptoms.

It was difficult to ward off an impending attack with any of these drugs. One child of 3 was given, as a preventive, 2 drams of the bicarbonate daily for four days before onset. Another child of 3 received for two days 4 drams of the bicarbonate daily, and for three days 3 drams of sodium citrate daily. So with three or four other cases.

In one fatal case dextrose (a 10 per cent. solution, 2 drams every three hours) was administered by rectum, but was not retained.

Once the vomiting had ceased, most of the children were placed on a simple diet low in fats. Beginning with such liquids as skimmed milk (with or without lime-water), rice-water, barley-water, oatmeal-water, orange-juice, grape-juice, we quickly added malted milk, cereals, crackers, toast, gruels and broths.

Lenhart¹³ believes that butter should be excluded, but not other fats. Koplik¹¹ reduces milk to a minimum. Langstein and Meyer (see Morse¹) have stated that a fatty diet is dangerous for children when there is disturbance of carbohydrate metabolism. Morse,¹ however, found that the variety of food seemed not to be a salient factor, although in some diseases, especially typhoid fever, in which the acetone bodies appear late, their presence was due to insufficient food or carbohydrates. To my mind, too great stress has been placed on providing a fat-free diet.

Other drugs we used symptomatically. Morphin was occasionally needed to control excitement. Saline solution was sometimes given by rectum. With sundry forms of medication that have been recommended I have had no experience. Let me enumerate a few:

1. Subcutaneous or intravenous injections of dextrose or levulose dissolved up to 10 per cent. strength in normal salt solution (Vander Hoof¹⁴).

2. Intravenous injection of salt solution (Fischl¹⁵).

3. Administration of glucose by mouth. Chalfant¹⁶ says this is unsatisfactory. Mellanby¹⁷ advises the administration of glucose rather than the attempt to "neutralize a series of acids, already fully neutralized and of no more significance than creatin."

4. Stomach lavage (Comby¹⁸).

13. Lenhart: *Cleveland Med. Jour.*, 1911, x, 1017.

14. Vander Hoof: *Charlotte Med. Jour.*, 1910, lxii, 257.

15. Fischl: *Pfaundler and Schlossmann's Diseases of Children*, 1912, iii, 171.

16. Chalfant: *Jour. Am. Med. Assn.*, 1912, lix, 852.

17. Mellanby: *Lancet*, London, 1911, ii, 8.

18. Comby: *Arch. de méd. d. enf.*, 1909, xii, 721.

5. Subcutaneous injection of sodium bicarbonate. Rachford¹⁹ advises 5 or 10 grains to the ounce. Experimentally, this has not proved serviceable (Rhamy¹⁹).

6. The administration of a mixture of sodium bicarbonate and lithium carbonate (Koplik¹¹).

7. Venesection. Withdrawal of 500 c.c. of blood. Introduction of 500 c.c. normal saline solution with 10 gm. of sodium bicarbonate (Houda²⁰). This may cause thrombosis (Marchand²¹).

8. Administration of pancreatin (Piper⁶ in operative cases).

REPORT OF CASE

Let me give a brief history of a severe case, typical of what we saw in this epidemic:

Patient.—A well-developed, phlegmatic boy, 2 years old, had had duodenal indigestion several times, but recently had been active, vigorous and in good health. He had had no previous attacks of acidosis. His diet had been well regulated with low fats. One other child lived in the same house, but otherwise the boy had not been intimately associated with children. For three or four days he had had a coryza and mild bronchitis.

Sudden onset occurred with vomiting at 5 a. m. The child continued to vomit at frequent intervals, especially if anything—even a little water—was taken by mouth. The vomitus became pale, watery and slightly yellow. With the aid of an enema he evacuated a semisolid brown stool—foul, slimy, acid. There was no diarrhea.

The temperature gradually rose to 103.5 F.; the pulse increased from 90 to 140. The boy's face was flushed with a contrasting whiteness about the mouth and nose. His breath came quickly, eagerly. One minute he was restless and uneasy, crying out for his mother, the next relapsing into stupor. In his waking moments he asked for water.

Examination. An examination made under difficulties showed coryza, a furred tongue, a retracted neck, pupils that were dilated but reacted to light, a slightly distended abdomen—nothing else. The urine was clear, strongly acid, with a specific gravity of 1.025, free from albumin and sugar. Acetone and diacetic acid were present. The white count was elevated but not remarkable.

Treatment was difficult and without material effect. As the hours passed the symptoms became more intense, the child's abdomen was noticeably retracted, his eyes sunken, his body wasted. Finally, toward midnight he had a convulsion and in a few minutes was dead.

In this particular case the necropsy, twelve hours post mortem, gave the following data:

Pathologic Examination (Macroscopic).—Body of a well-developed, well-nourished, white male child. Pupils equal, dilated.

Primary incision shows skin thin, abdominal fat very slight; muscle firm, normal color, non-bleeding.

Peritoneal cavity: Very little fat in omentum. Superficial veins of intestines not remarkable. Intestinal mucosa normal except for conspicuous glands. Stomach mucosa injected.

19. Rhamy: Jour. Am. Med. Assn., 1912, lviii, 628.

20. Houda: Jour. Am. Med. Assn., 1912, lviii, 1194.

21. Marchand: München. med. Wehnschr., 1912, lix, No. 4.

Liver 10 cm. below costal margin and 10 cm. below xiphoid. Extends upward to cartilage of fifth rib. Prominent areas, size of a bean, white in color, on anterior surface. Gray in spots on section.

Adrenals, pancreas and kidneys normal.

Brain: Adhesion of dura to pia in region of closed posterior fontanelle. Vessels prominent and congested. Surface of brain moist but without excessive fluid.

Pathologic Examination (Microscopic).—Liver: Fatty metamorphosis, edema, hemosiderin pigmentation.

Spleen: Acute hyperplasia.

Pancreas: Post-mortem degeneration.

Thymus: Atrophy. Necrosis and calcification of corpuscles of Hassal.

Stomach: Normal.

Appendix: Follicular hyperplasia.

Diagnosis: Fatty degeneration of the liver; congestion of the brain.

Cultures from the several organs were negative except one from the base of the brain. Here we cultivated two kinds of cocci. One was unusually large and occurred in pairs; its colonies were white. The other coccus was as large as staphylococcus; its colonies were translucent.

Antigen was made from the mixture, and from the larger coccus and from a culture of meningococcus. All of these gave a negative test with blood-serum from a second case of acidosis with auto-intoxication. We cannot rule out the possibility that the immune bodies which fix the complement had not yet developed in this serum.

By blood-culture we obtained from this latter case a coccus which was not identical with either of the cultures procured at autopsy. Numerous cultures made from throats and nasal discharges in other cases gave variegated growths from which no specific organism could be isolated.

GENERAL DISCUSSION

Acidosis has been defined as an "abnormal metabolism of carbon leading to the appearance of organic acids in the blood and urine, and the formation of ammonia to neutralize these acids" (Cautley¹²).

These organic acids, beta-oxybutyric and diacetic, with acetone, comprise the acetone bodies. It is said that oxybutyric acid is the precursor of diacetic acid and acetone the final product of the series; yet there is no good reason for so believing, except the order of their appearance in the urine, the similarity of their chemical formulas and the fact that diacetic acid, when heated, changes to acetone. Against this view is the fact that acetone can readily be formed from a number of other substances. Furthermore, the administration of sodium acetoacetate is followed by the elimination of beta-oxybutyric, just the reverse of the common understanding of their order of formation (Rhamy¹³).

When the total amount of acetone bodies formed is low, the percentage of acetone itself is high; when the total amount of acetone bodies is high, the percentage of acetone itself is low (Piper, in post-operative cases). If the excretion of acetone exceeds 0.5 gm. daily diacetic acid is present also. If the excretion of acetone exceeds 1 gm. daily, beta-oxybutyric acid is present (Beddard¹⁴).

Koplik²¹ has stated that acetone arises from the splitting of nitrogenous substances of the body. Von Noorden,²² however, says that though tissue destruction is a necessary factor, there is no evidence that acetone comes from the breaking down of proteids. It is readily obtained from fats and has been obtained from carbohydrates (Brackett²³). Knoop²⁴ has demonstrated the formation of acetone bodies from fatty acids. By feeding 100 gm. of oleic acid to a healthy man, Joslin (see Brackett, Stone and Low²³) caused an excretion of over 1,700 gm. of acetone in twenty-four hours, without producing other symptoms. Geelmuyden noticed acetonuria after adding olive oil and butter to a normal diet (Rhamy¹⁹).

The processes by which fat is burned are dependent on the simultaneous combustion of carbohydrates. The acetone bodies are probably excreted as a result of a lessened oxidation of fat, brought about either indirectly as a result of lessened sugar combustion, or by a direct influence of some unknown nature on fat combustion (Howland and Richards⁴). This direct influence, according to Guthrie,²⁵ is an intoxication produced by absorption of toxins from the intestines, by bacterial poisons — for example, pneumonia — or by inorganic poisons — for example, phosphorus. The liver, already laden with fat, becomes surcharged with more fat derived from the subcutaneous tissues. Should the overtaxed liver fail to metabolize the enormous quantity of fat thus brought to it, the circulation becomes flooded with the products of imperfect oxidation.

Brackett²³ states that although the presence of primary intestinal toxins has not been shown, it is probable that they exist, while Melanby¹⁷ suggests that such toxins arise directly at the portal area from intestinal infection or putrefaction.

The acetone bodies constantly appear in some lesions of the pancreas, which fact, too, is in accord with the intestinal origin of some cases of acid intoxication, since disturbance of pancreatic function would reduce digestive activity in the duodenum with resulting faulty cleavage of fats (Rhamy¹⁹).

We know that acetone is found in very small amounts in the urine of healthy children (Baginsky²⁶), never exceeding 1 cg. in twenty-four hours (Langstein and Meyer). Indeed, acetone and its associates, diacetic and oxybutyric acids, are possibly being constantly formed in minute quantities in normal metabolism (Rhamy¹⁹).

22. Von Noorden: *Clinical Treatises on Metabolism*. New York, 1903.

23. Brackett, Stone and Low: *Boston Med. and Surg. Jour.*, 1904, cli, 2.

24. Knoop: *Ztschr. f. d. gesammte Biochemie*, 1905, vi, 150.

25. Guthrie: *Brit. Med. Jour.*, 1908, ii, 1158.

26. Baginsky: *Arch. f. Kinderh.*, 1888, ix, 1.

In increasing amounts they are formed in many pathologic conditions: in starvation and cachexia; in eclampsia; in poisoning by phosphorus, salicylates and by other drugs; in hepatic lesions like acute yellow atrophy; in diabetes; in nervous disturbances due to fright; in the so-called delayed anesthetic poisoning. Sedgwick²⁷ and Smith²⁸ have called attention to the frequency with which their formation accompanies adenoids. Comby¹⁸ remarks that 50 per cent. of his series had appendicitis and believes that this is an etiologic factor that has been overlooked by other observers. Harris²⁹ notes their occurrence in scarlet fever. Gordon³⁰ (quoting Reiche) states that acetonuria was present in 60 per cent. of a series of thirty-two hundred diphtheria cases. Frew³¹ examined 662 out-patient children of whom 61.6 per cent. showed acetonuria. These were largely infectious cases and the nature of the concomitant infection seemed not to affect this ratio; except that in typhoid fever only 15.6 per cent. of the children showed acetonuria. Chalfant¹⁶ obtained positive results in 86.45 per cent. of his cases, affected with postoperative vomiting.

Morse¹ states that acetone bodies are present in the urine of infants and children under approximately the same conditions as in adults. They are often present in acute diseases accompanied by high fever (especially in the acute exanthems, diphtheria and pneumonia), vary, as a rule, directly with the height of the fever and disappear with the fall of the temperature. Morse has noted, also, the enormous increase of these bodies in children during convulsions, but thinks they are not the cause of the convulsions. Acetone bodies are rarely found in the urine in gastro-intestinal disorders of infancy but are commonly found during childhood, whether the disorders are acute or chronic. There may be no accompanying symptoms of acid intoxication.

In these instances, although a state of acidosis exists, with the acetone bodies present in the blood, the hydrogen ions are "rapidly neutralized by sodium in the tissue fluids, potassium in the cells, and by alkaline earths chiefly derived from bones. If this is not enough, the excess is neutralized by ammonia, derived from protein, which would normally have been metabolized into urea" (Cautley¹²). There is a consequent increase in the excretion of ammonia and a diminution in urea (Rhamy¹⁹). In children it is invariably true that acidosis in the body is accompanied by an increase in the excretion of ammonia (Langstein and Meyer).

27. Sedgwick: *AM. JOUR. DIS. CHILD.*, 1912, iii, 209.

28. Smith: *Lancet*, London, 1911, ii, 1186.

29. Harris: *Lancet*, London, 1910, i, 1346.

30. Gordon: *New York Med. Jour.*, 1913, xcvii, 529.

31. Frew: *Lancet*, London, 1911, ii, 1264.

"Should more acid be produced than can be thus neutralized, the reaction of the tissue fluids may be altered and cause symptoms of acid intoxication. It is therefore evident that acidosis may be very common, though acid intoxication is rare. It can exist long before the tissue fluids are rendered less alkaline and before toxic symptoms arise. One passes gradually into the other (Cautley¹²)."

It is said that acetone is non-toxic; it is argued that in "recurrent vomiting" acidosis can be prevented by the administration of dextrose and yet the acute symptoms occur just the same (Beddard⁷). Edsall⁹ has said that acetone and diacetic acid have little if any significance in producing symptoms, for neither is very toxic; that beta-oxybutyric acid, however, is more important and produces the only form of auto-intoxication. According to Piper,⁶ the acetone bodies, when excreted freely, are harmless. Injected intraperitoneally and subcutaneously into guinea-pigs, large amounts of acetone gave no anatomic lesions unless the administration was prolonged for many days (Brackett²³).

Despite the fact that the acetone bodies are only mildly toxic, the general conception is that oxybutyric and diacetic acids, by uniting with the fixed alkalies, reduce the alkalinity of the tissues and thereby produce a condition of toxemia. The amounts of these two acids are in constant relation and with acetone vary directly as the severity of the intoxication (Edsall⁹). The ammonia excretion is perhaps another index of the degree of intoxication, although Ewing³² found that in pregnancy the estimation of ammonia nitrogen did not follow this rule.

With the neutralization of the alkalies of the tissues, the blood can carry less carbon dioxid; there may be a decrease from the normal 24 per cent. to 3 per cent. Hence, carbon dioxid accumulates in the tissues until we have a condition of internal suffocation (Vander Hoof¹⁴).

At variance with this theory is Lenhart's¹³ view that while the blood is less alkaline to titration, this fact does not prevent it from carrying carbon dioxid. Venous blood will take up carbon dioxid and in acid intoxication the carbon dioxid of the tissues is not excessive. The carbon dioxid is an incident. Benedict,³³ too, while admitting that the alkalinity of the tissues cannot be inferred from that of the blood, has stated that in conditions other than diabetes the alkalinity of the blood may be lower than that ever observed in diabetic coma, without the appearance of the symptoms of intoxication.

Rachford¹⁰ has suggested that the acids, besides removing alkaline bases which are needed in metabolism, have a direct toxic action in that they bring poisonous alkaline bases (as ammonia) into the blood. Ewing,³² too, from his experimental work, has concluded that the intoxication may be due to the accumulating antecedents of urea. He

32 Ewing: *Arch. Int. Med.*, 1908, ii, 330.

33 Benedict: *Arch. f. d. ges. Physiol.*, 1906, cxv, 106.

adds that none of the principles of the theory of acid intoxication have been proved — namely, carbon dioxid asphyxiation, degeneration of the vital organs by withdrawal of alkalis and reduced alkalinity.

Partial reports of a dozen or more necropsies in children are available. In these the predominating lesion was enlargement and fatty infiltration of the liver. Other data were:

LANGMEAD,³⁴ CASE 1.—Kidneys fatty. No nephritis. Mucous membrane of posterior wall of stomach mottled by dark red areas of hemorrhage.

LANGMEAD, CASE 2.—No organism could be grown from the blood, spleen or bile. Nine c.c. of blood yielded 0.33 per cent. acetone.

LANGMEAD, CASE 3.—Three c.c. of blood yielded 0.24 per cent. acetone.

GRIFFITH,²—Necrotic changes in mucous membrane of stomach and intestine; slight parenchymatous alterations in pancreas, spleen and kidneys.

BRACKETT²³ (FOUR NECROPSIES).—Only marked lesion was extreme fatty degeneration of liver and muscles.

ABT.³⁵—Fatty degeneration of all the organs.

Rhany¹⁹ believes it is probable that there are essential changes in the blood-vessels, brain and excretory organs, ending in acute degeneration of the liver. Crile's³⁶ experiments would lead one to anticipate, also, changes in the adrenals.

Rosenfeld (see Langmead³⁴) showed that if animals were fattened on mutton-fat and then poisoned with phloridzin, acute fatty infiltration of the liver occurred and that the fat so deposited was mutton-fat. From this Langmead concludes that the liver condition is a result, not a cause. Brackett²³ thinks the adipose tissue of the body furnishes the fat in the liver.

There is evidence, then, that the acetone bodies are derived from fatty acids imperfectly metabolized in the liver; that this imperfect metabolism may be coincident with lessened sugar combustion; but that there is an immediate exciting cause for this imperfect metabolism.

Sometimes an intestinal disturbance is the only obvious exciting cause, and here we have the "digestive" type of acidosis. Again, we have primary poisoning from an inorganic poison, while in a third group one must consider a concomitant infection. In the "infectious" type, however, there may be intestinal disturbance, evidenced by diarrhea, foul stools and the like. The increased excretion of ammonia may be due not only to the incomplete metabolism of urea, but to the entrance through the portal circulation of a bacteriologic product accruing from putrefaction in the large intestine (Folin and Denis³⁷).

34. Langmead: Brit. Med. Jour., 1907, ii, 812; 1905, i, 350.

35. Abt: Am. Jour. Med. Sc., 1914, cxlvii, 86; Jour. Am. Med. Assn., 1910, lv, 991 (discussion).

36. Crile: Personal communication.

37. Folin and Denis: Jour. Biol. Chem., 1912, xi, 161.

In the Concord epidemic one saw acidosis with auto-intoxication in all degrees of severity; one saw both initial and recurrent cases. I believe that "acid auto-intoxication," "recurrent vomiting" and "cyclic vomiting" are merely degrees of an acidosis. The beneficial effects of alkaline treatment suggest that the symptoms are due to an excess of acid. In spite of the fact that the acetone bodies formed are apparently less in amount than those found in diabetes, their constant presence suggests, further, as Morse¹ has said, that they have an intimate relation with the symptoms; that they comprise, in fact, the acids causing this hyperacidity.

The Concord epidemic bore an analogy to the Birmingham epidemic reported by Parke.³⁸ It differed in that the Birmingham cases had an initial diarrhea, constant enlargement of the liver, absence of cyanosis and not infrequently absence of vomiting. Parke reported eighteen cases in infants under 20 months with an alarming death-rate (71 per cent.). It is also of interest that the symptoms in our epidemic were not unlike those attributed in several localities last year to the consumption of blighted chestnuts.

To the best of my knowledge an extensive epidemic similar to that in Concord has not heretofore been reported. With so few bacteriologic data I can offer slight evidence that any organism was the immediate exciting cause. Nevertheless, I believe that the prevailing respiratory infection was significant; that this infection was usually conveyed by direct contact; that it was selective and that some infected children did not develop acidosis.

My thanks are due to the several physicians whose cases are included in this compilation and to various officials at the Harvard Medical School who examined the bacteriologic and pathologic specimens.

38. Parke: *Jour. Am. Med. Assn.*, 1910, iv, 991; 1907, xlix, 1827.

A RESPIRATION INCUBATOR FOR THE STUDY OF THE ENERGY METABOLISM OF INFANTS*

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For the study of the metabolism of infants, especially new-born or premature infants, it is important to have perfect control of the temperature to which the child is exposed. Preliminary work on animals with a respiration chamber surrounded by water, the latter kept warm by means of a gas-flame placed underneath, convinced me that a more exact control was necessary before observations on the infant could be undertaken. In casting about for a satisfactory type of thermoregulator, the Freas oven came to mind and after conference with the inventor (Prof. Thomas B. Freas, Dept. of Chemistry, Columbia University) as to the feasibility of the application of his regulator to the purposes in hand, plans were agreed on for the construction of an electric incubator which would be suitable for the introduction of a respiration chamber large enough to contain an infant one year of age. Dr. Freas has placed the laboratory under special obligations for the interest he has shown in the execution of these plans.

This particular incubator measures 60 by 82 by 115 cm. outside and 46 by 48 by 100 cm. inside. It rests on a special iron stand provided with it, 85 cm. above the floor and makes a good appearance as a piece of laboratory or hospital furniture (Figs. 1 and 2).

The regular plan of construction of the Freas air thermostat¹ was departed from in only a few particulars. For example, it was necessary to have a considerable number of openings through the wall for the passage of the ventilating-pipes and cooling-coil, the introduction of thermometers, the connection of the oxygen regulator, etc. The range of temperature was fixed at from 20 to 50 C., the capacity of the heater being limited to 200 watts. The motor for driving the stirring-fan (Fig. 5, *F*) which is provided with the incubator was mounted on a large steel spring so that the vibrations should be damped out to some extent. The glass doors were made as large as the front

* From the Physiological Laboratory of the Cornell University Medical College, New York City.

1. Freas, Thomas Bruce: A Study of Thermostats, Dissertation, University of Chicago, 1911.

end, thus permitting plenty of light to enter and were provided with strips of felt so as to make the closure practically air-tight.

THE RESPIRATION CHAMBER

The chamber measures 30 by 32 by 76 cm. inside. It was made of 14-ounce tinned copper, strongly lock-jointed and soldered, and was rimmed at the front end by a heavy brass casting. Another casting of the same dimensions was made as a frame for the glass head or door of the chamber. The glass is held in place by litharge cement covered with heavy wax and a coat of white-lead. A heavy rubber gasket is

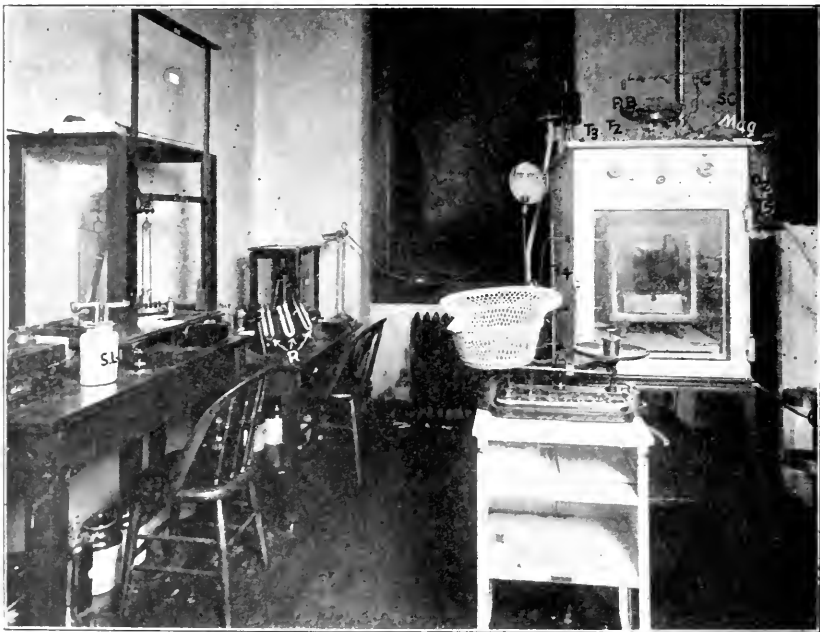


Fig. 1.—General view of room in Bellevue Hospital containing respiration incubator (Eimer and Amend) set up ready for use. The inner chamber is shown through the glass doors of the incubator. Inside the chamber the bed is seen. The balances on the left of the room are used in weighing the absorbers. The balance in the middle of the room (sensitive to 1 gm.) is used in weighing the infant. Further description in the text.

cemented to the brass rim, and a perfectly air-tight closure of the chamber is secured by clamping the frame of the head firmly against this gasket by means of twelve L-shaped steel bolts, which engage the back side of the brass rim (Figs. 2 and 3). The chamber is mounted on wooden runners and is strongly reinforced by means of three galvanized iron ribs girthing it at equal intervals from front to back.

Pressure changes inside or outside the chamber, therefore, do not alter its volume.

Since the incubator measures 46 by 48 by 100 cm. inside, a space 7.5 cm. wide is left on all sides of the chamber. The air in this space is kept in motion by a fan (Figs. 4 and 5).

VENTILATION AND MEASUREMENT OF RESPIRATORY EXCHANGE

The ventilation of the respiration chamber is accomplished by means of a Benedict "universal respiration apparatus,"² connected to it by means of wide rubber tubing and ½-inch brass pipes. The brass pipes are screwed into strong brass bushings soldered to the copper

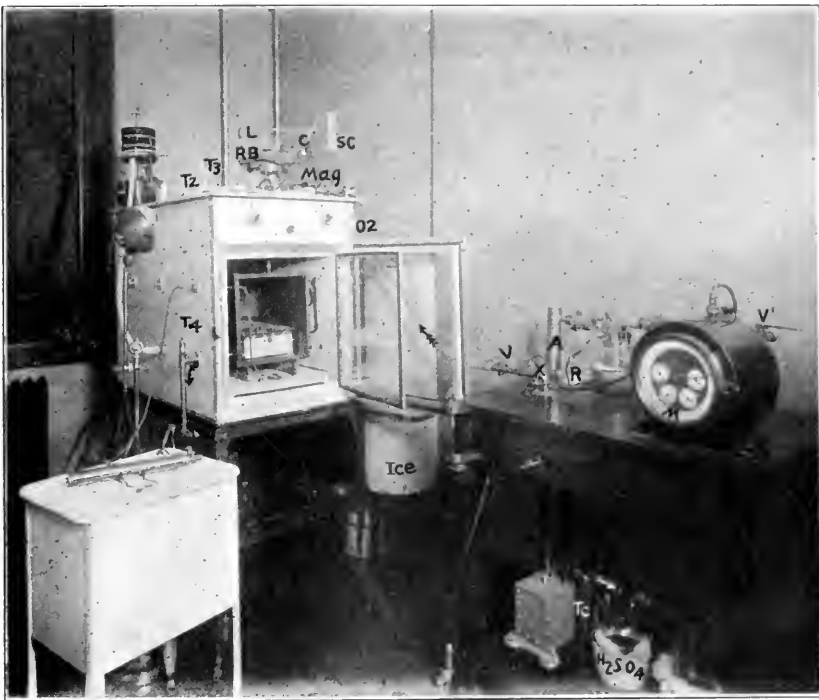


Fig. 2.—Another view of the same room. The absorber table is seen at the right. The glass doors are open and the glass head of the inner chamber is lying on the shelf below the incubator. The stethoscope tubes may be seen lying on the nurse's table and the bell of the stethoscope inside the incubator. Further description in the text.

wall. The inlet pipe enters at the upper back corner of the chamber on the right side and the outlet is connected with the lower front corner on the left. Thermometers are admitted to the inlet and outlet pipes by means of T joints (Fig. 3, T4). The arrows in Figure 2 show the direction of the air current.

2. Benedict, F. G.: *Am. Jour. Physiol.*, 1909, xxiv, p. 345; *Deutsch. Arch. f. klin. Med.*, 1912, cvii, 156; *AM. JOUR. DIS. CHILD.*, 1914, viii, 1.

The Absorber System.—The Benedict apparatus was so constructed for use with the incubator that by turning valves (V and V', Fig. 2) the absorbers could be quickly changed after stopping the blower, without the loss of more than 20 c.c. of air.[†] Each set of absorbers consists of two soda-lime jars for absorption of carbon dioxide and a sulphuric acid absorber for catching the water lost from the soda-lime. Each of these absorbers is small enough to be weighed (separately) on a Sartorius balance sensitive to 0.001 gm. The soda-lime absorbers are made on the plan (Fig. 1, S. L.) adopted for the absorbers used with the Sage calorimeter in Bellevue Hospital.³ The sulphuric acid

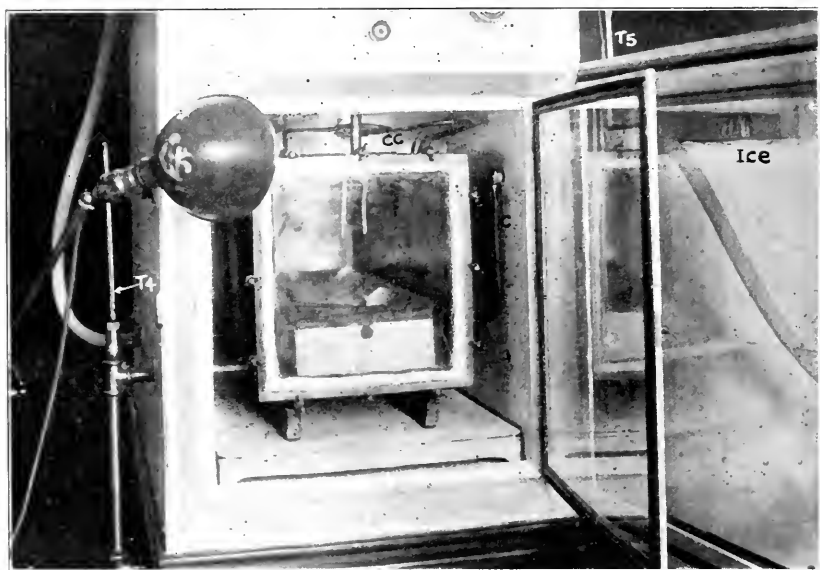


Fig. 3.—A near view of the interior of the incubator showing the cooling coil, c.c.

absorber is the gas washing-bottle designed by Williams⁴ for use with the animal calorimeter in this laboratory. Immediately following the sulphuric acid absorber is a brass tower containing sponges kept moist with very dilute sodium hydroxid solution, which serves the double purpose of imparting a slight amount of moisture to the air and of arresting any traces of acid fumes which may come from the drying-bottle.

Since the water given off from the lungs of the child does not enter into the computation of the heat production by the indirect method

[†] Since this was written the table has been reconstructed so two sets of absorbers can be connected at once and the change from one to the other accomplished with a single lever operating both valves.

3. Lusk, Soderstrom and Riche: Arch. Int. Med., to appear soon.

4. Williams: Jour. Biol. Chem., 1912, xii, 323.

(except as this water may affect the volume of the oxygen admitted), the absorbers used in the collection of this water are not weighed. They consist of two Williams bottles placed in series after the blower on the under part of the absorber table (Fig. 2, H_2SO_4). A brass trap (Fig. 2, *Tr.*), of a capacity about equal to the amount of the sulphuric acid contained in the first Williams bottle, is introduced for the safety of the blower. A bicycle coaster brake on the large pulley of the blower makes it impossible to turn the blower the wrong way; but the trap would catch any acid which might be drawn back by sudden blockade of the air-circuit at any point.

The Residual System.—The measurement of the oxygen absorbed by the child is based on the general proposition that oxygen be admitted to the air-circuit just as rapidly as it is used. This presupposes that the respiratory products should be absorbed and removed from the air as rapidly as they are produced. The efficiency of the absorbers is such that as far as the welfare of the child is concerned the ventilation is perfect. Neither carbon dioxide nor water vapor can accumulate to any appreciable extent. But an *absolutely* perfect adjustment of the rate of ventilation so as to leave the composition of the air *exactly* the same at the end of a period as at the beginning is impossible, especially if the child should cry or void urine near the end of the period. Since the admission of oxygen is regulated by the total volume of the air, (see below) and since this volume will vary with the amount of water vapor in it as well as with the temperature and barometric pressure, it is necessary to know the composition of the air at the close as well as at the beginning of a period. The analysis is carried out by diverting a measured sample of air from the main circuit, causing it to flow through a special set of absorbers and returning it to the system without loss of anything more than the small quantities of carbon dioxide and water contained in it. These analyses are called the residuals because they give information as to the amounts of the various gases residual in the air at definite moments.

A small copper pipe is tapped into the main circuit on the positive side of the blower (Fig. 2, *R*) and is led upward through the top of the table. By turning a stop-cock at the base of this pipe a small fraction of the total air current can be drawn off. The residual absorbers consisting of three U tubes (Fig. 1, *R*) (the first containing sulphuric acid and pumice stone, the second finely granular soda-lime and the third sulphuric acid and pumice stone again)⁵ are connected to this small pipe and the air having passed through them is conveyed to the meter (Fig. 2, *M*) where it is measured, thence through a drying-

5. Cf. Benedict and Carpenter: Carnegie Institution of Washington, Publ. 123, p. 73.

tower" (the meter contains water) and back to a point (Fig. 2, x) in the main system where the pressure is low.

The U tubes are weighed to the fourth decimal place before and after drawing off the sample. When the amounts of water vapor and carbon dioxide in this measured sample (usually 5 liters) are known, the total amounts in the entire system are readily calculated. By a series of corrections which will be better understood after the method of conducting an alcohol check is explained, the amount of oxygen residual in the air at the time the air sample is taken can also be computed.

The Oxygen System.—Oxygen is admitted into the ingoing air so that it may be thoroughly diffused into the chamber. The amount admitted is regulated by the method first described by Benedict and Carpenter⁷ and as slightly modified by Williams⁴ in his construction of the animal calorimeter. The essential parts of this arrangement consist of a rubber bag or spirometer which serves as a tension equalizer and volume indicator at the same time (Figs. 1 and 2, *RB*) and a magnet (*Mag.*), which, when actuated, releases pressure on a rubber tube leading from the oxygen cylinder (*O₂*). The rubber bag communicates with the respiration chamber by means of a brass pipe, and a valve in this pipe permits the bag to be shut off from the chamber. The oxygen cylinder⁷ while in use is suspended from a strong hook at the right side of the apparatus conveniently near the magnet. The magnet is connected through a resistance board carrying three lamps and through the mercury cups (*C*), situated on the horizontal arm above the magnet, with the house current. A lever (*L*) 38 cm. long is pivoted above the bag and is so counterpoised that it rests lightly on the bag by means of a broad metal disk. The arm ends at the right in a point which traverses a scale (*Sc*). It carries contact points which dip into the mercury as the lever descends. As the oxygen in the air of the circuit is used up by the child the bag collapses until the lever makes contact with the mercury (sparking is prevented by means of a condenser not shown in the figures). This actuates the magnet and releases pressure on the pure gum tubing leading from the oxygen cylinder. Oxygen thereupon enters the circuit until the volume is increased sufficiently to break the electric circuit, when pressure is again applied to the tubing thereby shutting off the oxygen; and so on.

6. The drying-tower is not shown in the figure because it stands behind the meter.

7. Purchased from the Consolidated Dental Mfg. Co., New York. These cylinders measure 4 cm. diameter by 33 cm. in length. They will contain about 50 gm. of oxygen under a pressure of 100 atmospheres. Together with the reduction valve the cylinder weighs about 1.5 kg. and can be weighed on the Sartorius balance to 0.001 gm.

At the beginning of a period oxygen is let into the system by hand until the pointer of the lever rests at a certain mark on the scale. At the end of the period the system is again filled to exactly the same point. If the volume of the air has not changed (by change of temperature, pressure, or composition of the air) the loss in weight of the cylinder would be the amount of oxygen consumed. Such conditions, however, would be very exceptional; hence all corrections must be made for every period.

Oxygen cannot be let into the system by any such automatic arrangement until the pressure which exists in the cylinder is reduced to a pressure which the rubber tube will withstand. A valve which reduces this pressure to a few pounds per square inch was made for these cylinders by the mechanician of the laboratory, Mr. James Evenden. It is shown in Figure 4.

Switch-Board.—A special switch-board, the end of which can be seen in Figure 6, provides electric outlets for: (1) the heater of the incubator; (2) the fan motor; (3) the motor on the absorber table; (4) the oxygen regulating system, and (5) any extra lamps required for illumination of the balances (Fig. 1), the interior of the incubator (Fig. 3), etc.

The Cooling-System.—The walls of the incubator being constructed of materials having a low coefficient of conductivity, the heat produced by the infant would not be conducted away as rapidly as produced and the temperature inside would rise unless the room air were at a very low temperature. To counteract this tendency and to furnish a chilling effect against which the heater of the incubator should operate, a cooling-system was installed. This consists of a coil (Fig. 3, *cc*) of copper pipe, $\frac{3}{4}$ inch inside diameter, making several turns on the two sides and the top of the inner wall of the incubator and carrying a stream of tap-water. At ordinary room temperature and with tap-water coming directly from the mains (that is, not warmed unduly by the house pipes) it is not necessary to chill the stream. It flows, however, through a coil of pipe inside an ice-tank (Figs. 1, 2 and 3), and in very warm weather the water can easily be kept down to the desired temperature by placing ice in contact with the coil. To secure a constant flow the water is given a constant head of pressure by passing it through a flush tank, operated by a ball cock, placed near the ceiling of the room. (This tank is too high to be seen in any of the figures, but the pipes leading to and from it are seen.) After passing through the cooling-system the water is conducted back to the sink.

A thermometer (Figs. 1 and 3, *T5*) is placed in the stream of water, and a wheel valve is placed near the tank, so that the cooling effect can be regulated to some extent both by the amount of ice and

by the rate of flow of the water. The thermoregulator of the incubator takes care of the finer regulation. The heater is sufficient to keep the space about the respiration chamber at 27 C., even when the water is at 4 C. and the rate of flow 400 to 600 c.c. per minute. This would be wasteful of electric current, however, and a water temperature of from 10 to 15 C. with a rate of 200 to 300 c.c. of water is more than sufficient to carry away the heat produced by a year-old infant even in very warm weather, unless the infant cries actively. In the latter case the speed of the water can be increased, or more ice can be introduced or

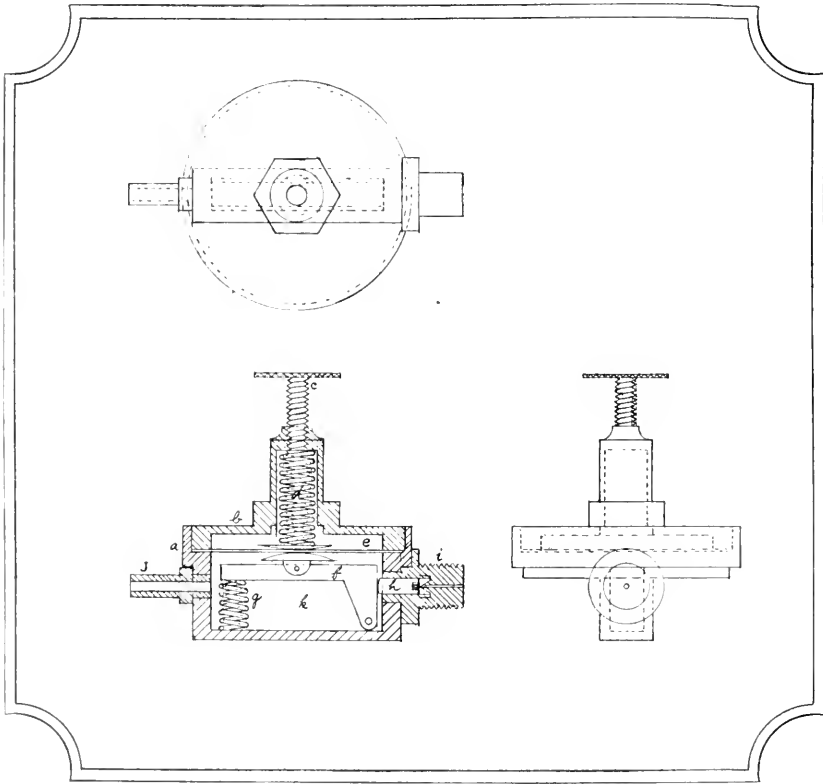


Fig. 4.—Detail of reducing valve used on small oxygen cylinder: *A*, case; *B*, lid of case; *C*, screw to compress spring; *D*, spring to reduce diaphragm; *E*, diaphragm; *F*, lever to close valve; *G*, spring to raise lever; *H*, valve with hard rubber tip to control oxygen; *I*, end to screw into oxygen cylinder; *J*, end for hose, oxygen supply. Oxygen contained in cylinder is held back by valve *H*. By compressing spring *D* with screw *C* lever *F* is lowered, thus allowing valve to come back and permitting oxygen to enter chamber *K* until the pressure beneath the diaphragm is sufficient to bring it to its original position which shuts off the oxygen again. When the oxygen in chamber *K* is below the desired pressure the tension of spring *D* again lowers the lever and repeats the operation.

the heater can be turned off. With such a cooling effect as just mentioned the temperature outside the chamber falls very quickly, and within a very few minutes also the temperature inside the chamber.

HEAT CONTROLS

Many control tests were made with the incubator as adapted in this way to the purposes of a respiration apparatus, both empty and with animals, before it was used with infants. Four thermometers are regularly used in the following positions: No. 1 (not shown in

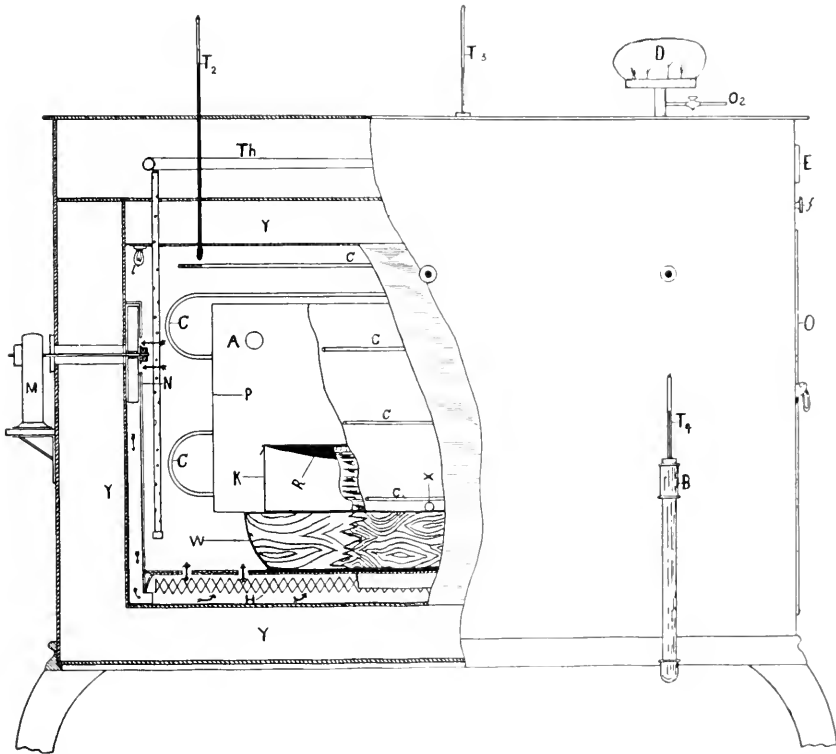


Fig. 5.—Sectional view of the incubator from the side. *Y*, asbestos packed wall; *H*, heater coil; *C*, cooling pipes; *P*, copper wall of inner chamber; *A*, point of entrance for air; *B*, exit pipe for air, containing thermometer; *W*, wooden runner which supports copper chamber; *K*, bed inside respiration chamber; *R*, rubber diaphragm; *Th*, thermo regulator; *M*, fan motor; *N*, fan. Arrows show direction of currents which equalize temperature inside the incubator. *D*, rubber bag for regulation of oxygen; *l*, lamp; *f*, control for setting regulator at any desired temperature.

any illustration) in the ingoing air; No. 2 on the top at the rear end of the incubator, the bulb extending into the outer air space; No. 3 (T_3 , Figs. 1, 2 and 5) on top near the center, the bulb extending 1 inch

into the inner air-space, and No. 4 in the outgoing air. All these thermometers are graduated to tenths of a degree C. and can be read to 0.05° . An air thermometer is usually kept on the wall near the absorber table.

Table 1 will serve as an example of the accuracy of the heat control. The subject was a small black dog, 4 kg. in weight, which lay perfectly still the entire hour.

TABLE 1.—HEAT CONTROL SUBJECT, SMALL BLACK DOG

| Time P. M. | Temperature | | | |
|---------------|--------------------|--------------------|------------------------------|--------------------|
| | Thermometer No. | Thermometer No. | Thermometer No. | Thermometer No. |
| | 1 | 2 | 3 | 4 |
| | Ingoing Air | Between Walls | Inner Chamber Near Center | Outgoing Air |
| | Degrees | Degrees | Degrees | Degrees |
| 1:50 | 23.0 | 27.0 | 28.1 | 27.9 |
| 1:55 | 23.1 | 27.2 | 28.1 | 28.0 |
| 2:00 | 23.1 | 27.2 | 28.1 | 28.1 |
| 2:05 | 23.2 | 27.3 | 28.1 | 28.1 |
| 2:10 | 23.3 | 27.2 | 28.1 | 28.1 |
| 2:15 | 23.4 | 27.2 | 28.15 | 28.1 |
| 2:20 | 23.5 | 27.1 | 28.15 | 28.1 |
| 2:25 | 23.5 | 27.15 | 28.15 | 28.1 |
| 2:30 | 23.5 | 27.15 | 28.15 | 28.1 |
| 2:35 | 23.5 | 27.1 | 28.1 | 28.15 |
| 2:40 | 23.5 | 27.2 | 28.1 | 28.1 |
| 2:45 | 23.6 | 27.0 | 28.1 | 28.1 |
| 2:50 | 23.6 | 27.0 | 28.1 | 28.1 |

The air temperature rose 0.6 of a degree during this observation and the temperature in the outer air space fluctuated somewhat according as the heat happened to be on or off at the moment of reading; but the temperature inside the inner chamber hardly varied at all during the entire hour.

CONTROL BY COMBUSTION OF ALCOHOL

The accuracy of the entire respiration apparatus has been checked many times in the course of the year and a half during which it has been in use, by combustion of alcohol in the chamber and the determination of the "respiratory quotient" of the flame. In the great majority of these check experiments all corrections have been made; but at times it has been sufficient to measure the oxygen by loss in weight of the cylinder with a correction for argon and the carbon dioxid by gain in weight of the absorbers without further corrections. With the flame burning uniformly the carbon dioxid residual in the circuit often does not change at all from the beginning to the end of a period. The water almost always falls the first period and then remains constant.

An example of a complete check experiment is given showing the manner of making all corrections. The same corrections and the same methods of calculation are used when the subject is a child.

Dec. 23, 1913. Alcohol check experiment.

Contents of respiration chamber — alcohol lamp and bed.

Vol. of air containing CO_2 67 l.
 Vol. of air containing H_2O 66 l.
 Vol. of air containing O_2 and N_2 69 l.

First period from 4:52 to 5:52 p. m.

At 4:52 residual analysis.

5 liters air contain 0.0178 gm. CO_2 and 0.0136 gm. H_2O
 67 liters air contain 0.238 gm. CO_2 (= 0.121 l.)
 66 liters air contain 0.179 gm. H_2O (= 0.223 l.)

To find residual O_2 .

Temperature 28.06 C.; barometer 765.1 mm.

log. 69 = 83885 0.121 l. CO_2 + 0.223 l. H_2O = 0.344 l.
 1
 log. $\frac{1}{1 + .00367(28.06)}$ = 95740
 765.1 = 00290
 log. $\frac{760}{760}$ 79915 = 62.973 l. at 0° and 760 mm.
 0.344 l. CO_2 and H_2O
 62.629 l. O_2 and N_2

Subtracting four-fifths for N_2 50.1032
 12.5258 l. O_2

At 5:52 residual analysis.

5 liters air contain 0.0178 gm. CO_2 and .0136 gm. H_2O
 67 liters air contain 0.238 gm. CO_2 (0.121 l.)
 66 liters air contain 0.129 gm. H_2O (0.223 l.)

To find residual O_2 .

Temperature 28.23 C.; barometer 765.3 mm.

log. 69 = 83885
 1
 log. $\frac{1}{1 + .00367(28.23)}$ 95719
 765.3 = 00302
 log. $\frac{760}{760}$ 79906 = 62.960 l. at 0° and 760 mm.
 .344 l. CO_2 and H_2O
 62.616 l. O_2 + N

Subtracting N with which exp'm't started, 50.1032
 12.5128 l. O_2

"Respiratory Exchange" Period 1

Gain in weight of CO_2 absorbers 4.850 gm.
 Loss in weight of O_2 cylinder... 5.060 gm.
 0.6 % correction for argon = 0.03 gm.

Loss in weight due to oxygen = 5.060 gm.

Residual analyses show: (1) no change in CO_2 of air but (2) amount of O_2 is less. (12.5258 — 12.5128 = .0130 l. = .0186 gm.) This shows that flame

used a little more O_2 than was admitted; therefore, $5.060 + .0186 = 5.079$ gm. O_2 actually used. Reducing weights to volume:

$$\begin{array}{r} \log. \text{ weight } CO_2 (4.850 \text{ gm.}) = 68574 \\ \log. \text{ weight to vol. } (CO_2) \quad \quad \quad 70680 \\ \hline 39254 = 2.469 \text{ l.} \\ \log. \text{ weight } O_2 (5.079) = 70578 \\ \log. \text{ weight vol. } (O_2) = 84496 \\ \hline 55074 = 3.554 \text{ l.} \end{array}$$

$$R. Q. = \frac{\text{Vol. } CO_2}{\text{Vol. } O_2} = \frac{2.469}{3.554} = .695$$

Second period from 5:52 to 6:52.

At 6:52 residual analysis.

5 liters air contain 0.0166 gm. CO_2 and .0114 gm. H_2O
 67 liters air contain 0.222 gm. CO_2 (= 0.113 l.)
 66 liters air contain 0.150 gm. H_2O (= 0.187 l.)
 $0.113 + 0.187 = 0.300$ l. CO_2 and H_2O .

Temperature 28.4 C. Barometer 765.3 mm.

$$\log. 69 = \quad \quad \quad 83885$$

$$\log. \frac{1}{1 + 00367(28.4^\circ)} = 95695$$

$$\log. \frac{765.3}{760} =$$

$$\begin{array}{r} 00302 \\ 79882 = 62.924 \text{ l. at } 0^\circ \text{ and } 760 \text{ mm.} \\ 0.300 \text{ l. } CO_2 \text{ and } H_2O \end{array}$$

$$\begin{array}{r} 62.624 \text{ l. } O_2 \text{ and N} \\ 50.1032 \\ \hline 12.5208 \text{ l. } O_2 \end{array}$$

"Respiratory Exchange" second period.

Gain in weight of CO_2 absorbers 4.968 gm.

Residual analyses show that CO_2 in air was less at 6.52 than at

$$5.52 \quad (0.238 - 0.222 = .016) \quad 4.968 \text{ gm.}$$

Actual amount of CO_2 given off = 4.952 gm. = (2.521 l.)

$$\begin{array}{r} \text{Loss in weight of } O_2 \text{ cylinder} \dots \dots \dots 5.500 \text{ gm.} \\ \text{Less 0.6 per cent. for argon} \dots \dots \dots .033 \end{array}$$

$$5.467 \text{ gm.}$$

Residual analyses show more O_2 in air at 6.52 than at 5.52

$$12.5208 - 12.5128 = .0180 \text{ l.} = .026 \text{ gm.}$$

$$\begin{array}{r} 5.467 \\ .026 \end{array}$$

Actual amount of O_2 used by flame = 5.441 gm. = (3.807 l.)

$$R. Q. = \frac{2.521}{3.807} = .662$$

$$\text{First period} \dots \dots \dots .695$$

$$\text{Second period} \dots \dots \dots .662$$

$$\text{Average} \dots \dots \dots .677 \quad \text{Theory } .666; \text{ error } 1.6 \text{ per cent.}$$

Table 2 gives the respiratory quotients obtained with the alcohol lamp for all the experiments between June 1, 1913, and July 1, 1914, on which all corrections could be made:

TABLE 2.—RESPIRATORY QUOTIENTS FOR EXPERIMENTS BETWEEN JUNE 1, 1913, AND JULY 1, 1914

| Date | Quotient | Date | Quotient | Date | Quotient | Date | Quotient |
|---------------|----------|--------------|----------|--------------|----------|--------------|----------|
| 6/ 5/13 | 0.654 | 1/ 5/14 | 0.652 | 1/20/14 | 0.664 | 2/ 9/14 | 0.684 |
| | 0.675 | 1/ 8/14 | 0.642 | | 0.656 | | 0.644 |
| | 0.655 | | 0.628 | | | | 0.641 |
| | | | 0.667 | Average... | 0.660 | | |
| Average... | 0.661 | Average... | 0.646 | | | Average... | 0.656 |
| 7/30/13 | 0.669 | 1/11/14 | 0.661 | 2/ 3/14 | 0.656 | 3/ 4/14 | 0.645 |
| | 0.670 | | 0.671 | | 0.653 | | 0.637 |
| | | | | | 0.644 | | |
| Average... | 0.669 | Average... | 0.666 | Average... | 0.651 | Average... | 0.641 |
| 12/ 1/13 | 0.617 | 1/16/14 | 0.741 | 2/ 5/14 | 0.673 | 6/24/14 | 0.627 |
| | 0.724 | | 0.610 | | 0.631 | | 0.666 |
| | | | 0.638 | | 0.644 | | |
| Average... | 0.670 | Average... | 0.663 | Average... | 0.649 | Average... | 0.642 |
| 12/23/13 ... | 0.695 | | | | | 7/29/14 | 0.652 |
| | 0.662 | | | | | | |
| Average... | 0.677 | | | | | | |

It will be seen that a perfectly theoretical result not infrequently occurs in a single period, but that often one period shows a high and the succeeding one a low result, the mean being very near to the theoretical value. This in most instances is due to a rise or fall of temperature near the end of the first period. The average error for all of the daily averages is 1.8 per cent.

CONTROLS WITH DIABETIC DOGS

Dogs completely under the influence of phlorhizin or deprived of the pancreas have a total incapacity to oxidize glucose. This results in a respiratory quotient⁸ which varies but slightly from 0.69. The diabetic dog, therefore, is a suitable subject for controlling the efficiency of a respiration apparatus of this type. The apparatus here described has been used in the study of certain problems in connection with pancreatic diabetes.⁹ The following are examples of the quotients obtained on dogs which were known from the relation of dextrose to nitrogen in the urine to be completely diabetic:

| | | | | |
|---------|----------------|-------|-------------|------|
| Dog VI. | July 9, 1913. | R. Q. | 11.27-12.27 | .68 |
| | | | 12.27- 1.27 | .68 |
| Dog C. | July 23, 1914. | R. Q. | 3.42- 4.27 | .69 |
| | | | 4.27- 5.13 | .68 |
| | | | 8.03- 8.49 | .68 |
| Dog E. | Aug. 4, 1914. | R. Q. | 5.27- 6.27 | .683 |
| | | | 8.27- 9.27 | .685 |

8. With the depancreatized dog this level is not invariably reached until about the fourth or fifth day after operation. Cf. Verzar: *Biochem. Ztschr.*, 1914, *xlxvi*, 75.

9. Murlin, Edelman and Kramer: *Jour. Biol. Chem.*, 1913, *xvi*, 79 and Kramer and Murlin; *ibid.*, 1914.

Animal experiments of this kind furnish a better control of the efficiency of the apparatus for work with infants than does the alcohol flame, for the reason that both the chemical and the physical properties of the air are more nearly like those of an experiment with the child. As a matter of course, the entire air circuit is thoroughly sterilized by means of formaldehyd, circulated by means of the blower, before the apparatus is used with the infant.

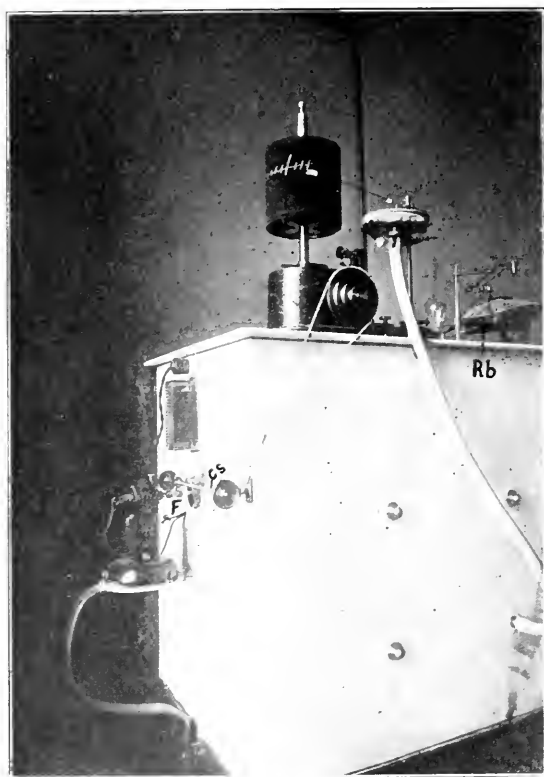


Fig. 6.—View of the rear end of the incubator showing fan motor (*F*); counter shaft (*CS*) for driving kymograph, and large recording tambour (*T*) for registering movements of the infant. *Rb*, rubber bag for equalizing tension and regulating flow of oxygen into the circuit.

OXYGEN BLANK

This form of control, introduced by Williams,¹⁰ has been found useful as a check on the gas analysis. It consists in sealing up the chamber, starting the blower and taking off a sample of air just as in starting a period for an alcohol check, but without a subject or lamp in the chamber. If the air which is thus closed in the circuit is some-

10. Williams: Jour. Biol. Chem., 1912, xii, 346.

what moist, the water absorbers will remove the water and its place will be taken by oxygen from the cylinder. The same would happen if the temperature were permitted to fall. At the end of an hour another sample of air is taken for analysis, and after the corrections for temperature and pressure are made, the amount of water lost from the air, as indicated by the residual analyses, should be equal to the amount of oxygen which has been lost from the cylinder. In such a check conducted on June 22, 1914, the amount of oxygen admitted was 0.346 liter in one hour. The air lost 0.411 liter of water; the carbon dioxid did not change. The temperature had risen 0.2° and

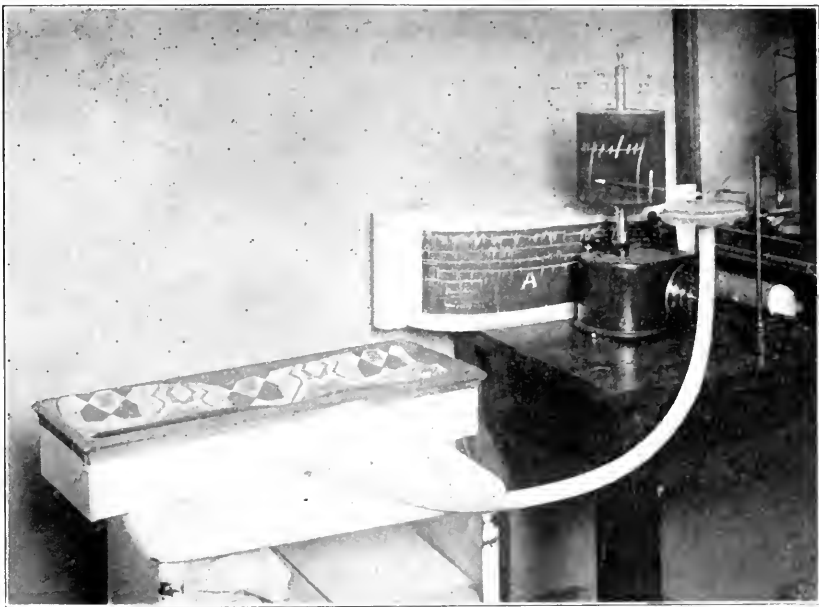


Fig. 7.—Rubber bed used for recording motions of the child, showing the wide tube and large tambour necessary for quick transmission. The character of the tracings obtained is seen in the open book (A).

the barometer had remained stationary. The temperature change caused an expansion of 0.056 liter in the entire system which would serve to keep out that much oxygen. Hence $(0.346 + .056 =) .402$ l. of oxygen, with no temperature change, would have been admitted to replace a (calculated) shrinkage of 0.411 liter.

REGISTRATION OF MUSCULAR ACTIVITY OF INFANT

The fan motor can be utilized for driving a kymograph situated on top of the incubator (Fig. 6). A small counter-shaft (*cs*) driven by a worm gear working on the axle of the fan carries a small pulley at

its outer end and this connects directly with the driving pulley of the kymograph.

For recording the actual motions of the infant several devices have been employed.¹¹ One of them employed with new-born infants consists of two large tambours connected by wide rubber tubing (Fig. 7). One of these tambours is the infant's bed while in the respiration chamber. The other (6 inches in diameter) carries a lever which writes directly on the smoked paper.

The bed consists of a galvanized iron box (10 by 22 by 61 cm.) covered with a piece of rubber sheeting. The rim of the box over which the sheeting fits is so made that the rubber comes in contact successively with two surfaces, each about 1 cm. broad, before it reaches the outside surface of the box itself. The corners, of course, are all rounded. An air-tight joint was secured by means of thick alcohol shellac. After the joint had been coated heavily with the shellac, the box was left for some days inverted on the rubber surface and weighted. Then the second surface was treated in the same way and the rubber tied firmly with a heavy cord. After several days' drying it was found to be air-tight. As a receiving plate for the infant's body a piece of linoleum of appropriate size was cemented to the upper surface of the rubber sheeting. A light blanket placed over this made a very comfortable bed.

Every motion of the infant was transmitted as an air wave to the recording tambour. In fact, the only objection to the device was its extreme sensitiveness. Even the pulsations of the air caused by the ventilating blower were recorded (Fig. 7 A). With older infants¹² the bed was discarded and the muscular motions were recorded by means of a cuff on the leg and a very flexible pneumograph placed about the chest.

11. See following papers.

12. See paper by Murlin and Hoobler to appear in this journal shortly.

INTRAVENOUS INJECTION OF DIPHTHERIA ANTITOXIN IN CHILDREN *

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The benefits of the antitoxin treatment of diphtheria are well recognized. From 1878 to 1894 in New York City the deaths from diphtheria per hundred thousand of population ranged from 110 to 264 and from 1890 to 1895 the combined diphtheria deaths in the larger European and American cities from 66.9 to 80.4 per hundred thousand population, while following the general use of diphtheria antitoxin since 1895 the deaths per hundred thousand of population have varied in New York City between 22 and 91, and between 19 and 55.6 in the larger cities of the world.

Diphtheria antitoxin was first used generally in 1895 and in 1896 first manifested its real value in the United States. Gradually fewer deaths from diphtheria have occurred, but it must be evident that in the past few years the death-rate has not been decreased materially. That we still have some deaths due to the disease is too well known. When deaths occur in patients having received antitoxin we generally believe them due to one of three causes: late administration of antitoxin, injection of insufficient amount of antitoxin, or the presence of exceptionally virulent diphtheria bacilli. Knowledge of these facts, however, is of little value in some of the cases of diphtheria seen, for any one having charge of diphtheria patients in a hospital for contagious diseases or doing consultation work in the diseases of children meets with patients who have had diphtheria for some days, but have had little or no diphtheria antitoxin administered. No wonder, then, that the need for further investigation of the treatment of diphtheria should be recognized and that any method which enables diphtheria antitoxin to exert its influence at the earliest possible time after administration should be tried.

We know that it is through the blood that antitoxin is distributed to the places where it binds toxins, and last year Park¹ reported from his experiments that he believed 5,000 units introduced intravenously are as beneficial as 20,000 units injected subcutaneously. His experiments showed that six hours after injection the blood-serum contains twenty units per cubic centimeter of blood when injected intravenously

* Received for publication Nov. 10, 1914.

1. Park: Boston Med. and Surg. Jour., 1913, clxviii, 73.

and two when given subcutaneously, and after twenty-four hours twelve units when given intravenously and six when injected subcutaneously.

Intravenous injection of diphtheria antitoxin was long ago practiced, but has usually not been followed because the subcutaneous method gives good results and intravenous injection is difficult in children. The veins of the arm are often too small, so in this series antitoxin was administered by way of the external jugular vein. Martha Wollstein² reported obtaining blood for cultures from children

TABLE 1.—GENERAL RESULTS OF DIPHTHERIA ANTITOXIN INJECTIONS

| | Subcutaneous Injection | | Intravenous Injection | |
|--|--------------------------------------|---------|---|---------|
| | | Average | | Average |
| Day of disease on which injections were made.. | 3, 8, 10, 3, 8, 7, 5 | 6.3 | 1, 3, 2, 2, 3, 2, 6, 10, 3, 3, 3, 10, 7, 3 | 4.1 |
| Units injected at one time | $3,000 \times 2$ $5,000 \times 7$ | 4.555 | $5,000 \times 10$ $10,000 \times 6$ | 6.875 |
| Number of injections made | 9 | 1.3 | 16 | 1.1 |
| Days after injection on which fever and membrane were absent and patients felt well..... | 13, 6, 4, 5, 10 | 7.6 | 2, 1, 3, 2, 1, 2, 1, 2, 4, 2, 2, 3 | 2.1 |
| Days after injection on which diphtheria bacilli were absent | 30, 36, 43, 16, 8 | 26.6 | 12, 8, 14, 2, 8, 2, 5, 5, 4, 6, 4, 6 | 5.4 |
| Total days sick..... | 15, 20, 12, 15, 15 | 15.4 | 3, 4, 5, 4, 4, 4, 7, 12, 14, 5, 5, 10 | 6.4 |
| Total days confined..... | 31, 44, 38, 22, 37 | 34.4 | 18, 20, 22, 11, 16, 14, 11, 23, 26, 7, 16, 13 | 16.4 |
| Carriers | | 4. | | 0. |
| Serum reactions | | 0. | | 4. |
| Immediate reactions..... | 0 | | 4 | |
| Deaths | | 2. | | 2. |
| Laryngeal diphtheria.... | | 2. | | 7. |
| Paralysis { Cardiac | | 3. | | 0. |
| { Palatine | | 1. | | 1. |

by going into the jugular vein and the method she suggested was employed in the cases reported here. In all, fourteen children received intravenous injections of diphtheria antitoxin. The results and symptoms observed are compared with those obtained in the same epidemic by subcutaneous injection in seven cases. The latter patients were seen in consultation and some had received diphtheria antitoxin before they were seen by me. The general results are shown in Table 1.

2. Wollstein, Martha, and Morgan, Edward: Blood Cultures During Life in Infants and Young Children, with Description of a New Technic, *AM. JOUR. DIS. CHILD.*, October, 1912, p. 197.

It is evident that so small a series does not offer enough evidence on all of the facts detailed. It seems fair, however, to draw some conclusions from the data. It will be observed that following intravenous injections the fever and membrane disappeared sooner and the patients felt well; that diphtheria bacilli disappeared more rapidly; that there were fewer carriers and that paralyses were less frequent than when subcutaneous injections were made.

Two children died in each series; death occurred from seven to fourteen hours after the first injection in each case. All four children who died had laryngeal diphtheria, but there were seven cases of laryngeal diphtheria in the series that received intravenous injections, and only two in the series given subcutaneous injections.

Reactions, however, followed only intravenous injections. The data in regard to this are shown in Table 2. These reactions are classified as "immediate" and "serum" reactions.

TABLE 2.—INTRAVENOUS INJECTION REACTIONS

| Immediate Reaction | | Average | Serum Reaction | | Average |
|----------------------------------|------------------------------------|----------|--|------------------------|----------------|
| Time after serum injection | 1, 1, 1½, ½ hrs. | 1 hour | Days after serum injection | 9, 10, 10, 6 | 8.8 |
| Temperature elevation | 103.2, 104 103.8, 103.2 | | Rash | | 4 cases |
| Disappeared in... | 3 hrs., 20 hrs. 5 hrs., 20 hrs. | 12 hours | Glandular enlargement | | 1 case |
| Respiratory distress | 2 cases | | Articular pain.. Days on which symptoms disappeared | 2, 2, 2, 3, 1 | 1 case 2.25 |

"Immediate Reaction."—Generally, the introduction of diphtheria antitoxin is not believed to be followed by an elevation of temperature, but slight elevations do occur frequently. When given intravenously, four injections out of sixteen were followed in from one-half to one and a half hours by striking symptoms. These were usually ushered in by a marked chill, then an elevation of temperature from 103.2 to 104 F., and in two cases by respiratory distress. All of these symptoms disappeared in from three to twenty hours, when the patients usually felt entirely well. That these were serum reactions did not seem to be the case, as in none did the later serum rashes appear. When serum rashes and reactions did occur they did not differ from those following other serum injections, though none occurred in the small series of patients receiving subcutaneous injections.

SUMMARY

It is not to be inferred that intravenous injections are advocated in all cases, but intravenous injections undoubtedly produce results more rapidly and so are to be preferred in late and severe cases.

Intravenous injection is less painful at the time of administration and later, and because of the smaller number of units necessary intravenous injection is much less expensive. Entrance into the jugular vein in children is not difficult and this vessel affords a ready site for the intravenous injection of diphtheria antitoxin when the median basilic and the cephalic veins are too small. This small series indicates that there are fewer carriers and heart failures are less likely to occur following intravenous injection, but there are more immediate and serum reactions. The immediate reactions never impressed us as being grave and in themselves did not seem to be a contra-indication to intravenous injection of diphtheria antitoxin.

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THE SUGAR-CONTENT OF THE BLOOD IN CHILDHOOD*

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In the last few years our knowledge concerning sugar in the circulating blood has made considerable advances.¹ The keen interest aroused by the questions concerned with glycemia has led to the perfection of numerous methods which in turn have resulted in greater numbers of cases being studied. The importance of the study of the blood-sugar is well emphasized by Scott,² who says:

Glycemia offers a more satisfactory indication of the condition of mobile sugar than does glycosuria; first because either an increase or a decrease in the amount of sugar may be demonstrated, while normal urine can show only an increase; secondly, because profound changes in glycemia may occur in response to conditions which do not produce glycosuria; thirdly the blood is in much more direct relation to the living cells than is the urine.

Though the variety of methods used has led to slightly divergent readings, it may be stated that the blood-sugar in the normal adult is about 0.09 per cent., varying from 0.06 to 0.12 per cent., and remains remarkably constant between these limits. Anything above 0.12 per cent. should be considered hyperglycemia. Such increase above the normal in the blood sugar has been found after taking food—the so-called alimentary hyperglycemia. As examples of this, Bing and Jacobsen,³ who consider 0.13 the highest normal level for the fasting adult, found that after taking 100 gm. of sugar by mouth the percentage in the blood rose to about 0.2 after one to two hours. Goetzky⁴ also found that the blood-sugar reached its maximum one-half hour after eating and then gradually descended to reach normal level again about three hours later. Though all investigators are not in absolute agreement as to these data, nevertheless these are important points.

* Received for publication Oct. 10, 1914.

* From the Laboratory of Physiological Chemistry of Cornell Medical School; the Pediatric Dispensary of Mount Sinai Hospital, and the Sanitarium for Hebrew Children at Rockaway Park.

1. Retzlaff, Karl: *Neuere Arbeiten über den Blutzucker*, Med. Klin., 1914, Nos. 19 and 20.

2. Scott, E. L.: *Content of Sugar in the Blood under Laboratory Conditions*, Am. Jour. Physiol., 1914, xxxiv, 306.

3. Bing, H. J., and Jacobsen, B.: *Blutzuckeruntersuchungen unter normalen und einigen pathologischen Verhältnissen*, Deutsch. Arch. f. klin. Med., cxiii, 571.

4. Goetzky, F.: *Der physiologische Blutzuckergehalt beim Kinde nach der Mikromethode von Bang*, Ztschr. f. Kinderh., 1913, ix, No. 1.

for in making any determinations, cognizance of the time of the preceding meal must be taken. Beside alimentary hyperglycemia, an increased blood-sugar is also found under various pathologic conditions, including diabetes, certain cases of nephritis, fever and after hemorrhage.

As far as infants and children are concerned, until relatively recently the sugar content of their blood had not been investigated for the reason that not only were the existing methods extremely cumbersome and tedious, but also too great a quantity of blood was needed for analysis. In the last few years, however, several new methods have been elaborated by which both of these drawbacks are overcome. The micro-method devised by Ivar Bang⁵ requiring but a few drops of blood, naturally removed the greatest hindrance to the study of the sugar content of the blood of infants, and as a result we are now in possession of a series of cases in which this question has been studied.

Coblner,⁶ Goetzky,⁴ Bing and Windelow⁷ and Mogwitz⁸ have examined a series of infants and have shown that in general the blood-sugar content is about the same as that of adults (0.07 to 0.11). In starvation the blood-sugar sinks to about half its former value (Mogwitz). Infants also show alimentary hyperglycemia which is more marked after taking sugar than after starch, probably because the latter is more slowly absorbed from the gastro-enteric canal.

The micro-method of Bang, which was the one used in all the determinations on infants and children, aside from the fact that the extremely minute amount of blood used and the resultingly small quantity of sugar actually determined would seem to allow of a large error in the results obtained, is moreover a rather complicated method, requiring much special apparatus. It constitutes, therefore, a scientific and laboratory method rather than a clinical one.

Through the kindness of Professor S. R. Benedict, I was enabled to make use of a method which has been devised by himself and Dr. R. C. Lewis, which not only has the advantage of requiring a relatively small amount of blood (though not so small as the Bang method), but also is one of extreme simplicity. The method depends on the fact that when a sugar solution is heated with a saturated solution of picric acid in the presence of an alkali, a definite colorimetric reaction results, the depth of the color being directly proportional to the quantity of sugar present. The method as used by me is a modification by Lewis

5. Bang, Ivar: *Der Blutzucker*, Wiesbaden, 1913.

6. Coblner, S.: *Blutzuckeruntersuchungen bei Säuglingen*, *Ztschr. f. Kinderh.*, 1910, i, 207.

7. Bing and Windelow: *Blutzuckerbestimmungen bei Kindern*, *Ztschr. f. Kinderh.*, 1913, ix, No. 1.

8. Mogwitz: *Ueber den Blutzucker der Säuglinge*, *Monatschr. f. Kinderh.*, 1913, No. 9.

and Benedict of their method published⁹ in 1914. A description of the method in detail follows:

A little more than 2 c.c. of blood is drawn from the vein at the elbow and placed in a small beaker. With an Ostwald pipet, 2 c.c. of the blood is then transferred to a 25 c.c. flask in which has been put 6 c.c. of distilled water. The pipet is rinsed out once with 2 c.c. of distilled water. The flask is then filled to the 25 c.c. mark with a saturated solution of picric acid. The heavy precipitate is now filtered off and a clear yellow filtrate obtained. Eight c.c. of this filtrate is transferred to a 20 cm. Jena glass test-tube, and to this is added 2 c.c. of a saturated solution of picric acid, 1 c.c. 10 per cent. sodium carbonate solution, two drops of petroleum oil (liquid albolene) and four small glass beads. This is then heated just to dryness directly over a Bunsen flame. The beads and the oil prevent the solution from "bumping" and frothing. The residue is redissolved in 5 or 6 c.c. of water and the solution brought to a boil. The mixture is then quantitatively poured into a 10 c.c. flask through a small bit of cotton wool in a funnel in order to remove the oil. The test-tube is washed with a few cubic centimeters of water and this is added to the contents of the flask, which is then cooled to room temperature and filled up to the 10 c.c. mark with water. The solution is then ready to be examined in the colorimeter. Its color is compared with a freshly prepared standard sugar solution, or, better, with a solution of picramic acid.¹⁰

The calculation of the blood-sugar is made as follows: Originally, 2 c.c. of blood was taken and made up to 25 c.c.; but only 8 c.c. of the filtrate was used; therefore, the sugar actually determined was that in 0.65 c.c. blood. If, as an example, the reading of the unknown solution is 12.0 when 0.00065 gm. sugar solution reads 10.0, we find the amount of blood-sugar present as follows:

$$\frac{10.0}{12.0} \times \frac{1}{10} = 0.083 = \text{the percentage of sugar in the blood.}$$

With this very simple method by which a determination can be made within fifteen minutes, it seemed worth while to examine a series

9. Lewis, R. C., and Benedict, S. R.: A Method for the Estimation of Sugar in Small Quantities of Blood, *Proc. Soc. for Exper. Biol. and Med.*, 1914, xi, 57.

10. The standard solution of picramic acid is made up as follows: 0.065 gm. picramic acid is dissolved in about 25 c.c. water; 0.1 gm. sodium carbonate is added and the solution warmed until all the acid is dissolved. The solution is then made up to 1 liter with distilled water. The color of this solution is permanent and is standardized against a known solution of sugar treated by the method above outlined. It was found that when a sugar solution containing 0.00065 gm. sugar (dextrose) was treated by the method and put in the colorimeter set at 10.0, its color exactly corresponded to the picramic acid solution set at 10.0. The picramic acid solution was therefore used as a standard set at 10.0, at which it was considered to equal 0.00065 mg. sugar.

of bloods obtained from children. In all, sixty children were examined. Of these twenty-six were normal. The remainder, as may be seen from Table 2, were suffering from a variety of complaints. The ages of the children varied from 2 to 14 years. The children were examined from two and one-half to three hours after eating breakfast, so that any postprandial hyperglycemia might be avoided. The temperature in all the cases but one (No. 55) was normal. None of the children showed glycosuria.

TABLE 1.—BLOOD-SUGAR DETERMINATIONS IN TWENTY-SIX NORMAL CHILDREN

| Case No. | Age, Years | Sugar, Per Cent. |
|----------|------------|------------------|
| 1 | 2 | 0.085 |
| 2 | 3 | 0.089 |
| 3 | 4 | 0.084 |
| 4 | 5 | 0.098 |
| 5 | 6 | 0.108 |
| 6 | 6 | 0.092 |
| 7 | 7 | 0.072 |
| 8 | 7 | 0.073 |
| 9 | 8 | 0.100 |
| 10 | 8 | 0.093 |
| 11 | 8 | 0.113 |
| 12 | 8 | 0.085 |
| 13 | 8 | 0.088 |
| 14 | 9 | 0.104 |
| 15 | 10 | 0.093 |
| 16 | 10 | 0.079 |
| 17 | 10 | 0.085 |
| 18 | 11 | 0.098 |
| 19 | 11 | 0.093 |
| 20 | 11 | 0.078 |
| 21 | 11 | 0.108 |
| 22 | 11 | 0.086 |
| 23 | 12 | 0.080 |
| 24 | 12 | 0.084 |
| 25 | 14 | 0.105 |
| 26 | 14 | 0.073 |

In the series of normal children (Table 1) the percentage of sugar varies from 0.072 to 0.113; in other words, it does not vary from the percentage found in adults. The only other series of blood determinations in children above infancy which I was able to find in the literature is that published by Goetzky¹ in 1913. He used Bang's micro-method on one hundred normal infants and children and found the average percentage of sugar in the blood of thirty-three children between the ages of 2 and 12 years to be 0.102, the extremes being 0.087 and 0.118. My own findings are somewhat lower, as may be seen from the following synopsis of Table 1:

| Age | Percentage | | |
|--------------|-----------------|----------------|---------------------------|
| 2-5 years. | 0.084 to 0.098. | Average 0.089. | Goetzky's findings 0.097. |
| 6-9 years. | 0.072 to 0.113. | Average 0.091. | Goetzky's findings 0.105. |
| 10-14 years. | 0.073 to 0.108. | Average 0.087. | Goetzky's findings 0.104. |

That the age of the child does not seem to influence the sugar content is shown by the fact that the youngest children, from 2 to 5 years old, had an average of 0.089 per cent., those from 6 to 9 years an average of 0.091, and finally, those from 10 to 14 years an average of 0.087 per cent. These results, moreover, do not corroborate Goetzky's finding that the percentage of sugar is slightly higher in older children than in the younger. Sex had no influence on the readings.

TABLE 2.—BLOOD-SUGAR DETERMINATIONS IN VARIOUS ABNORMAL CONDITIONS

| No. Case | Years Age | Disease | Per Cent. Blood-Sugar |
|----------|-----------|-------------------------------------|-----------------------|
| 27 | 11 | Compensated mitral regurgitation. | 0.088 |
| 28 | 9 | Compensated mitral regurgitation. | 0.085 |
| 29 | 9 | Compensated mitral regurgitation. | 0.091 |
| 30 | 12 | Compensated mitral regurgitation. | 0.076 |
| 31 | 10 | Compensated mitral stenosis. | 0.095 |
| 32 | 12 | Decompensated mitral regurgitation. | 0.068 |
| 33 | 12 | Decompensated mitral regurgitation. | 0.069 |
| 34 | 12 | Decompensated mitral regurgitation. | 0.060 |
| 35 | 10 | Endocarditis; adherent pericardium. | 0.062 |
| 36 | 9 | Neurotic. | 0.108 |
| 37 | 13 | Neurotic. | 0.085 |
| 38 | 10 | Neurotic. | 0.104 |
| 39 | 11 | Neurotic. | 0.074 |
| 40 | 13 | Orthostatic albuminuria. | 0.111 |
| 41 | 9 | Orthostatic albuminuria. | 0.093 |
| 42 | 10 | Orthostatic albuminuria. | 0.124 |
| 43 | 12 | Chronic nephritis. | 0.089 |
| 44 | 14 | Chronic nephritis. | 0.094 |
| 45 | 6 | Adenoids. | 0.089 |
| 46 | 10 | Facial tic. | 0.072 |
| 47 | 13 | Chorea. | 0.117 |
| 48 | 7 | Chorea. | 0.060 |
| 49 | 6 | Chorea. | 0.072 |
| 50 | 5 | Cyclic vomiting (during attack). | 0.104 |
| 51 | 9 | Cyclic vomiting (between attacks). | 0.082 |
| 52 | 10 | Cyclic vomiting (between attacks). | 0.096 |
| 53 | 9 | Intestinal indigestion. | 0.088 |
| 54 | 3 | Measles. | 0.080 |
| 55 | 4 | Malaria (temperature 106.2°). | 0.087 |
| 56 | 12 | Progressive muscular dystrophy. | 0.078 |
| 57 | 11 | Tuberculous hip. | 0.098 |
| 58 | 6 | Tuberculous hip. | 0.106 |
| 59 | 7 | Tuberculous knee. | 0.091 |
| 60 | 9 | Convalescent meningitis. | 0.080 |

In Table 2 will be found the readings taken on the blood of children suffering from various ailments. It will be seen that in general there is no great departure from the normal figures. Patients 27 to 35 are children suffering from cardiac complaints of various kinds. Those whose hearts were fully compensated (Nos. 27 to 31) gave normal readings; whereas those showing failure of the circulation gave very low readings (Nos. 32 to 35). Two of these severely ill cases had albuminuria and all four had enlarged livers. The case of endo-

carditis, adherent pericardium and ascites (No. 35) presented considerable cyanosis, but the blood-sugar was low, 0.062, which is unusual since cyanotic cases have been found to show a mild hyperglycemia.

Three cases of orthostatic albuminuria were examined and all three gave high readings. Bing and Jacobsen,³ who report a blood-sugar determination in a young girl of 16 with this urinary anomaly, found no variation from the normal figure. No conclusions can be drawn from three cases, but the high results are certainly interesting, especially in view of the fact that some cases of nephritis also show a hyperglycemia.

In a case of malaria, the blood examined one hour after the chill, when the temperature was 106.2, showed a normal sugar value.

Of particular interest are the cases of cyclic vomiting. In this condition, in which numerous factors in the urine examination point toward a disturbance of carbohydrate metabolism, a deviation from the normal in the amount of sugar in the blood might be anticipated. As may be seen in the table, however (Nos. 50 to 52), the figures for the blood-sugar are well within the normal limits. Patients 51 and 52 were examined between attacks while in apparently good health, their urine showing no trace of acetone. Patient 50, on the other hand, was seen on the fourth day of a typical attack of cyclic vomiting with marked acetonuria. The child, who had retained nothing, not even much water, looked very pale and appeared considerably prostrated. He was examined at 10 a. m. and had taken nothing by mouth since the evening before, when he had been given some milk which was promptly vomited. The blood-sugar was found to be 0.1040.

The blood-sugar in only one other case of cyclic vomiting has been studied: Hilliger¹¹ published a case of a 6-year-old girl in whom severe attacks of vomiting with great amounts of acetone in the urine could be brought about at will by withdrawing all the carbohydrate from the diet. At such times the blood-sugar, which previously had been 0.13 and 0.14, dropped within twenty-four hours to 0.073. Control children subjected to a similar withdrawal of carbohydrate from the diet failed to show any such change in the blood-sugar, the value remaining 0.13 and the children showing no signs of nausea or vomiting. These results are open to the criticism that the values found for the controls as well as for the subject of the experiment between attacks of vomiting are extremely high, being distinct examples of hyperglycemia. Since another author (Goetzky), working with the same method, obtained very much lower readings on many normal

11. Hilliger, G.: Ueber periodisches Erbrechen mit Acetonaemie, *Jahrb. f. Kinderh.*, 1914, lxxx, No. 1.

children, the figures obtained by Hilliger in his vomiting case must be accepted with reserve. My own case shows an exactly opposite condition to that of Hilliger, for a percentage of 0.104 after so long a period of fasting would apparently point to a relative hyperglycemia, since, as pointed out by Mogwitz, the blood-sugar in starvation may fall to one-half its normal value. Further studies are being made in this case which will be reported on later.

The remaining cases are mostly those of children convalescing from different illnesses and show no variation from the normal.

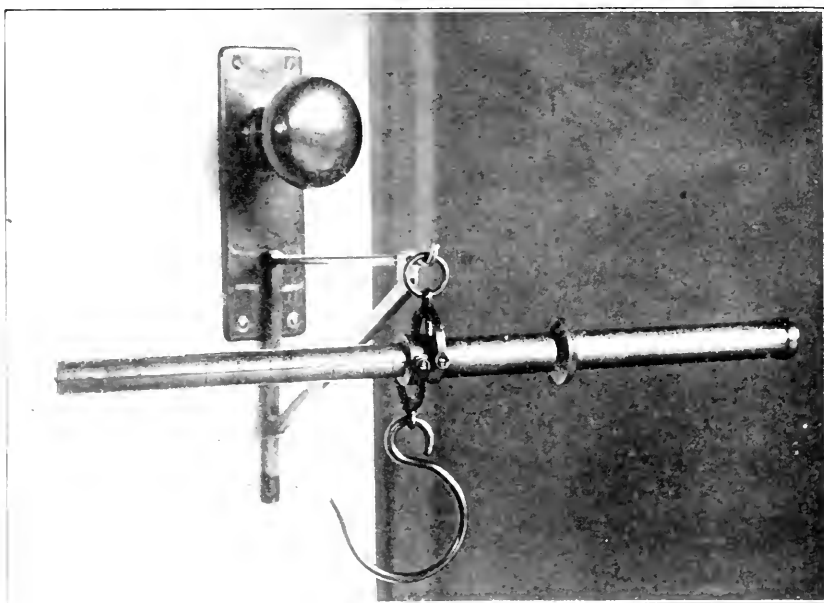
In conclusion I wish to express my thanks to Professor S. R. Benedict for his kindness in placing this method at my disposal and for numerous helpful suggestions offered in the course of the work.

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A POCKET BABY SCALE *

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Every physician who has had to do with infant-feeding in private practice has realized the need of a means of ascertaining the weight of these little patients conveniently and accurately. In many families scales are to be found and records of the babies' weights are kept ; but



A pocket baby scale.

usually no scale is available, or none is found that is sufficiently sensitive for all purposes. My experience with babies who are partially breast-fed and partially bottle-fed led me to search the market for a scale that would, by weighing the infant before and after nursing, show the amount it obtained from the breast. Any scale found that approached the necessary accuracy was so bulky and so poorly adapted to the purpose that I undertook to devise one to overcome these objections.

* Received for publication Nov. 20, 1914.

The one here described I have found satisfactory in every way. The principle of the old-fashioned steelyard is employed, the beam being so constructed as to telescope. The device, except the yokes and bearings, is made of brass, the telescoping core sliding through the tube in either direction. The divisions marked on the core represent pounds, while the scale on the tube is divided into ounces and quarters of an ounce, as indicated by the rider which traverses the entire length of tube. The yokes and bearings are of tempered tool steel and so constructed as to be sufficiently sensitive and yet insure unlimited service. A sight projecting from the tube and ranging with the arms of the upper yoke shows when the beam is level and in balance. A bracket whose members hinge and fold up closely is made to support the scale. The horizontal member of the bracket, when passed through the key-hole of a door, so engages as to hold it rigidly, thus leaving both hands free to attend to the weighing. The process then is as follows: The baby, slung in its napkin, is hung on the large hook; the core is slid to the mark indicating the number of pounds, and the rider completes the balance and indicates the ounces and fractions of an ounce. The capacity is 20 pounds. The scale and bracket are enclosed in a case measuring $1\frac{1}{2}$ by 3 by 8 inches and altogether weigh 2 pounds.

Children's Memorial Hospital.

PROGRESS IN PEDIATRICS

REVIEW OF PROGRESS IN OPHTHALMOLOGY

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PREVENTION OF MYOPIA

Risley's well-known studies of refraction among the children of Philadelphia public schools in 1881 showed the presence of a high percentage of errors. Correction of these defects (and his results have been confirmed by others) proved the value of glasses not only in relieving symptoms and giving more acute vision but also in preventing increase of refraction. In other words, he has demonstrated that myopia is often acquired by the near use of uncorrected hyperopic astigmatic eyes.

The continued use of astigmatic eyes at the near point demands constant accommodation and convergence effort, and thus the eyes are laterally compressed by the internal and external recti muscles and are maintained in the state of refraction adapted to 13 inches, that is, a temporary myopia of 3 D. The combined effect of these two causes, especially in individuals who have inherited a tendency to stretching of the sclera, is to change the hyperopic astigmatism into myopic astigmatism at the opposite axis, and then by continuation of the use of the eyes under unchanged conditions the eyes become myopic in all meridians.

Risley's later publications (1913) of examination of nearly seven thousand eyes shows a steady decrease in the percentage of myopia. The moral to be drawn from this careful study of statistics and the truths clearly shown by them, is the necessity for the examination of all children's eyes under cycloplegia, and the accurate correction by glasses of errors of refraction. The modern class-rooms, the better distribution of light, the improved paper and print, and the stricter attention paid nowadays to the hygiene of the pupils and to the elimination from the schools of students with contagious conjunctivitis, contribute in no small degree to the betterment of both eyes and health.

During the present year the Committee of Conservation of Vision of the Pennsylvania State Medical Society has substantially aided the cause by having printed and permanently placed in schoolbooks used in Philadelphia public schools many thousand circulars, stating in easily understood language rules for the care of the eyes. The pre-

vention of myopia — and incidentally of some functional diseases and possibly of organic eye disease — is of incalculable value to any community.

PHLYCTENULAR KERATITIS AND CONJUNCTIVITIS

Phlyctenular keratitis and conjunctivitis in young persons are said to be ocular manifestations of tuberculosis. In order to determine the etiology of these two common affections the family history and the associated clinical appearances are of importance. The specific tests, such as von Pirquet's, while not alone sufficient to indicate general tuberculosis, are valuable sign-posts. In order that the skin reaction to tuberculin shall be reliable great care must be exercised, both as to the remedy itself and as to its method of application.

I exhibited at the Ophthalmic Section of the College of Physicians of Philadelphia four patients with suspected tubercular keratitis. In three the response to inoculation was prompt and strongly positive. In the fourth the reaction was negative, although general indications of diluted tuberculosis, such as swollen glands and malnutrition, were not wanting. The test was repeated in the negative case with greater accuracy and thoroughness and showed a strong reaction.

Boer¹ illustrates with cases the frequency with which a diagnosis of ocular tuberculosis may depend on the clinical appearance although the tubercle bacillus may not be demonstrated in the local lesion, and animal inoculation may prove negative. One case was that of a 21-months-old child, who during a severe conjunctivitis developed a thickening of the upper lid, which increased after recovery from the conjunctivitis. The condition was unilateral, ran a chronic course and was accompanied by marked thickening of the tarsus. The von Pirquet test was positive, and microscopic examination of excised tarsal tissue showed typical tubercles.

Butler² regards phlyctenular ophthalmia as the result of a "tuberculo-toxemia." A tuberculosis etiology was exceedingly probable in 70 per cent. of his cases. He has found that the symptoms disappear without other treatment within a couple of days after one injection of T. R.

Stephenson³ in speaking of the diagnosis says that the advantages of the von Pirquet method are that it is safe and easily performed and is thus applicable for out-patients. On the other hand, the test is so sensitive, and tuberculosis past or present so common, that except in young children the positive reaction is not of much diagnostic use. The negative reaction is of greater value.

1. Boer: *Arch. f. Ophth.* (Graefe's) lxxxv, 1913, 273, 293, 362.

2. Butler: *Brit. Med. Jour.*, Oct. 18, 1913.

3. Stephenson: *Lancet*, London, Nov. 29, 1913.

The Koch subcutaneous test gives both a general and a focal reaction. Stephenson draws one important distinction between the etiology of infection of the external portions, the conjunctiva, cornea and lacrimal apparatus, and infection of the iris and choroid and other parts of the interior of the eye. As a rule, he says, the former are exogenous, while the latter are endogenous. These facts are of value in prognosis, for while a tuberculosis lacrimal sac may be excised with good hope of extirpating the disease, excision of the eye with tubercle of the iris or choroid is likely to be of little value in eradicating or even in checking general tuberculosis.

On the other hand, phlyctenular ophthalmia is often a benign and transient complication or accompaniment of nasopharyngeal disease. Practitioners of extended experience and particularly those who commenced practice before the results of laboratory examinations were considered conclusive or even dependable, can remember cures effected by the removal of adenoids or enlarged tonsils to increase oxygenation of the blood, by restricted and nourishing diet and by the elimination of sources of intestinal irritation, and locally by astringent washes and emollient applications. Cobbledick⁴ is convinced that adenoids are always present and claims that the result of promptly removing them, and, if necessary, the tonsils, is "magical." Further, any tendency to recurrence is said to disappear after the operation.

OPHTHALMIA NEONATORUM

The desirability of legislative enactment to prevent the ravages of ophthalmia neonatorum by early treatment has led to the formation of committees of medical men in many of the states of the United States. In Pennsylvania a law was passed about twelve or fifteen years ago requiring notice within six hours by midwives of redness of the lids or discharge from the conjunctiva in the new-born. In case of non-observance of this law a fine of two hundred dollars or imprisonment was to be exacted. Apparently the law in Pennsylvania — and this is equally true of other states — becomes a dead letter unless breakers of the law are convicted. In the few weeks following a conviction the number of cases reported increases amazingly and then it gradually drops off until a new violation is discovered and the culprit punished. New measures will probably be no more effective unless all avenues for the escape of violators be closed, and this fact should not be forgotten by the framers of the laws.

The following paragraph⁵ from the *Journal of the American Medical Association* is apropos here:

4. Cobbledick: *Brit. Med. Jour.*, Nov. 22, 1913.

5. *Jour. Am. Med. Assn.*, Oct. 17, 1914, p. 1392.

The prevention of this disease, so serious for the babe's future, is not attained by discussing the value of eugenics, or attempting the regulation of prostitutes, or demanding the always non-successful reporting of gonorrheal cases. It will be more certainly secured by insisting that every physician and every midwife (by continued and repeated instruction) shall use Credé's method, namely, to instil into each eye of every new-born babe two drops of a 2 per cent. solution of silver nitrate. Every eye inflammation in the new-born, or occurring shortly after birth, should be considered ophthalmia until the microscope shows that it is an innocent inflammation. If the gonococci are found, the little patient should be placed in the care of a skilled oculist.

It must be borne in mind that gonococci are not essential to the production of purulent ophthalmia and that their absence does not always prove that the eye is free from danger. On the contrary, many cases of severe ophthalmia bearing all the clinical signs of gonorrheal inflammation but without laboratory confirmation lead to ulceration and destruction of the cornea. At times one may be led to suspect carelessness or ignorance of the microscopist, so inconsistent are his findings with the violence of the symptoms.

Holloway⁶ writes:

It is now quite generally known that many of these cases are non-gonorrheal in origin, and for reasons that are obvious, the proportion of gonorrheal cases, both in and out of institutions, necessarily varies according to the social and moral character of the patients.

From the studies of Stephenson, Mayou and others, it is safe to assume that 60 per cent. to 65 per cent. of the cases owe their origin to a Neisser infection, although some recent writers, for example Sattler (*Am. Oph. Soc.*, 1913) concede but 50 per cent. We thus see that many of these cases may be regarded as cases of purulent ophthalmia analogous to those seen in association with some of the infectious diseases of children.

PROPHYLAXIS

Sattler says:

We have a fairly reliable prophylaxis for non-specific organisms, but a next to impossible one for specific or gonococci. The latter infection will continue undisturbed its destructive work and defy the best prophylactic measures at present at our command and claim their quota of infantile eyes.

Notwithstanding this pessimistic statement, and in view of the unquestioned truth that the number of cases of ophthalmia of the new-born has been enormously reduced since the almost universal adoption of the Credé method, it becomes the duty of every obstetrician to sterilize both the birth canal and the infant's eyes.

1528 Walnut Street.

6. Holloway: *Ophth. Rec.*, December, 1913.

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THE ENERGY METABOLISM OF TEN HOSPITAL CHILDREN

BETWEEN THE AGES OF TWO MONTHS AND ONE YEAR *

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INTRODUCTION

In a study of the energy requirement of the new-born child by Bailey and Murlin,¹ it has been shown that when exposed to a temperature between 26 and 29 C. the sleeping infant falls far short of producing as much heat per unit of body surface as does the adult. It was seen also that a thin baby produced more heat per unit of surface and much more per unit of weight than a fat baby of the same age placed under exactly the same circumstances. These differences were so striking as to suggest a further study of the metabolism of children of different weights and of different ages, with special reference to the influence of body fat on the heat production. Aside from hereditary influences on the body size, the chief cause of difference in weight of normal infants at birth, or, for that matter, at any other given age, is the proportion of fat, which in turn is determined by the nutritive condition. Does this fat, deposited for the most part beneath the skin, reduce the metabolism per unit of weight because it protects against heat loss by radiation and conduction, or because it serves as so much ballast, so to speak, thereby cutting down the proportion of active tissue where heat is produced?

This question of the proportion between the active and the inactive tissue, and its influence on heat production has been raised wherever marked discrepancies have been found in the application of Rubner's law of surface area. Rubner,² himself, when he first observed such discrepancies in the application of this law (at that time but recently demonstrated for animals) to human subjects of different ages, hinted at a difference of functional capacity, but dismissed the idea as one of

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1. Bailey and Murlin: *Proc. Soc. Exper. Biol. and Med.*, 1914, xi, p. 109; also *Am. Jour. Obst.*, February, 1915.

2. Rubner: *Zuschr. f. Biol.*, 1885, xxi, 397.

minor importance. Magnus-Levy and Falk,³ however, in their study of the influence of age on the respiratory metabolism very clearly expressed the possible significance of differences in this proportion.⁴ Again, in his work on myxedema, Magnus-Levy⁵ raises the question whether the lower metabolism of patients suffering with this disease may not be due to the fact that they have actually a smaller functioning mass of protoplasm.

In his work with Heubner on infants, Rubner⁶ explains every difference in the metabolism per unit of surface as due to differences in the dynamic action of the food or to differences in muscular activity, and does not consider the difference in the amount of body fat possessed by their well-nourished infants as compared with their atrophic one. Schlossmann,⁷ however, although a firm believer in the application of Rubner's law even to atrophies, in answering the criticisms of Kassowitz is obliged to admit that the law presupposes a normal amount of subcutaneous fat.⁸

Placing the emphasis on the heat production rather than on the heat loss, Howland⁹ also limits the law of surface area to the "well and moderately nourished" children, holding that "it does not seem to apply for the greatly emaciated child with almost complete absence of muscular tissue."

The subject has received extended consideration for the first time at the hands of Benedict and Talbot¹⁰ in their monograph on the "Gaseous Metabolism of Infants." Comparing the sleeping metabolism of sixty-one different infants¹¹ varying in nutritive condition from

3. Magnus-Levy and Falk: *Arch. f. Anat. u. Physiol.*, 1899; *Phys. Abth. Suppl. Band*, p. 314.

4. Thus: "Wir gehen wohl nicht fehl, wenn wir dem als Todtes Reserve und Heizmaterial im Bindegewebe und Nervensysteme eingelagerten Fette (wie auch dem Glykogen) jeden eigenen Umsatz ganz absprechen, wenn wir den Knochen und dem Bindegewebesgerüste nur einen geringen zuerkennen, und den grössten Betrag des Kraftumsatzes und des Gaswechsels den protoplasmareichsten Geweben, den Muskeln, Drüsen u. s. w. zuteilen. Dass die Gewichtseinheit des Protoplasmas des Trägers thierischer Functionen im kindlichen Alter einen erheblich höhern Umsatz zeigt als in der Zeit vollen Reife geht ja aus den absolut hohen Zahlen der Kinder klar hervor."

5. Magnus-Levy: *Ztschr. f. klin. Med.*, 1904, lii, 201.

6. Rubner: *Ztschr. f. Biol.*, 1899, xxxviii, 375 et seq.; also *Ztschr. f. exper. Path. u. Ther.*, 1905, i, 18 et seq.

7. Schlossmann: *Ztschr. f. Kinderh.*, 1912-'13, v, 227.

8. "Die Voraussetzung dabei ist natürlich einmal eine relative Norm der Umgebung, zum andern aber eine relative normale Oberfläche des Kindes. d. h. eine funktionierende und gut passende Haut mit dem normale Fettgehalt der Unterhaut" (p. 231).

9. Howland: *Tr. XV Internat. Cong. Hyg. and Demog.*, Washington, 1912, ii, 448.

10. Benedict and Talbot: *Carnegie Institute of Washington, Publ.* 201.

11. Benedict and Talbot: *Studies in the Respiratory Exchange of Infants*, *Am. Jour. Dis. Child.*, July 1914, p. 1.

extreme atrophy to "very much overweight" and in age from a few hours to 17 months, they find no parallelism between the heat production and body surface, as given by any of the known formulas, and none between the heat production and body weight. They conclude that it is the "active mass of protoplasmic tissue which determines the fundamental metabolism." The only measure of this which they propose, however, is one of proportion between age on the one hand, and weight and height on the other. Thus by comparing children having the same weight and height, but of different ages, their results show that the older child invariably has the higher metabolism, the reason given being that in order to have the same weight as a younger child, the older must have relatively less body fat and therefore relatively more active tissue.

Before it was known to us that Benedict and Talbot were engaged on this problem plans had been made by us to carry through a comparison of the heat production amongst a similar assortment of infants, using as an expression of the proportion of fat to active tissue the specific gravity of the child's body, as nearly as this could be determined.¹²

12. The method developed in Pfaundler's laboratory by Kastner (*Ztschr. f. Kinderh.*, 1912, iii, 391) for obtaining the volume of the child's body was adopted as the most practicable method available, but it yields only approximate results. In fact, no method of obtaining the volume of the living body exclusive of the air of the lungs and air passages is at this time possible for children who are too young to control the respiration at the will of the observer. Nevertheless, it was possible to get on successive days good duplicate readings for the volume of the body up to the chin by displacement of water, if patience enough were exercised to secure absolute quiescence on the part of the child; and measurement of the head by Kastner's method was found by controls made on eight cadavers of infants in this hospital to be fairly accurate. The "approximate specific gravity" as determined in this way did tend to equalize the metabolism per unit of weight. (Cf. *Proc. Soc. Exper. Biol. and Med.*, 1914, xi, 115). This seems, however, to have been mere coincidence, or else there is some relation between chest capacity and size of head (the two factors most difficult to estimate accurately) on the one hand and the amount of fat on the other. Two other methods of determining the volume of the child's body have been attempted. Both were suggested by Pfaundler's discussion (*ibid.*, iii, 413) of a somewhat similar method. One of these consisted in running a known amount of water into a flask set inside the closed inner chamber of the incubator and noting the rise in pressure on a manometer communicating with the inner space, (a) with the child inside and (b) with the child not inside. A direct proportion then would subsist between the inner volumes with and without the child and the changes in pressure. The original volume of the empty box being known the volume of the child would be obtained by difference. The second method consisted in raising the pressure by admitting oxygen from the oxygen cylinder; but instead of attempting to admit the same amount of oxygen with the child in the box and with the box empty, the attempt was made to produce the same rise in pressure both times and then to calculate the volumes from the amount of oxygen lost from the cylinder, as determined by weighing, in the two measurements. The chief difficulty in both cases lay in the lag of the thermometers indicating the air temperature. Either method can be employed while the child sleeps without disturbing him in any way.

The discovery of comparatively recent analyses on the actual composition of the bodies of normal, atrophic and fat infants by Sommerfeld, Steinitz¹³ and Steinitz and Weigert¹⁴ have made it clear to us, however, that the *actual specific gravity cannot vary sufficiently to account for differences in metabolism*. Moreover, the constancy of the percentage of nitrogen in children of different weight was a distinctly surprising discovery, the significance of which will be commented on in the final discussion of results. Table 1, compiled from various sources, exhibits the variation in actual composition of the child's body in widely different states of nutrition.

TABLE 1.—COMPOSITION OF INFANT'S BODY COMPILED FROM VARIOUS AUTHORS

| Author | Condition | Age | Weight | In 100 Parts | | | | |
|---------------------------|-----------------|---------------------------|--------|--------------|----------|-------------|------|------|
| | | | | Water | Dry Sub. | Ether Extr. | Ash | N. |
| Cammerer and Soldner..... | Normal new-born | Av. of six infant at term | 2,820 | 71.8 | 28.2 | 12.3 | 2.7 | 1.8 |
| Sommerfeldt | Normal infant | 3 months | 4,340 | 79.15 | 20.85 | 13.4 | 2.73 | 2.27 |
| Steinitz No. III..... | Atrophic infant | 3 months | 2,625 | 79.9 | 20.1 | 1.45 | 2.73 | 2.3 |
| Steinitz No. IV..... | Atrophic infant | 2½ mos. | 1,960 | 82.3 | 17.7 | 1.8 | 3.2 | 2.13 |
| Steinitz No. V..... | Atrophic infant | 3¾ mos. | 3,220 | 79.8 | 20.1 | 1.98 | 3.34 | 2.51 |
| Steinitz and Weigert..... | Fat infant† | 4 months | 3,711 | 58.94 | 41.06 | 24.17 | 2.98 | 2.25 |

* Cammerer and Soldner: Ztschr. f. Biol., 1902, xliii, 1.

† Sommerfeldt: Arch. f. Kinderh., 1900, xxx, 253.

‡ This child had been fed by its mother on gruels containing a large preponderance of carbohydrates.

It is obvious from these figures that fluctuations in the amount of fat are offset by fluctuations in the content of water; in other words, that fat instead of replacing protein or being added to the other constituents of the body, actually replaces water, leaving the percentage of protein the same. Calculated to a fat-free basis, these infants had very nearly the same content of water.

From these analyses may be calculated the actual specific gravity of a normal, an atrophic and a very fat infant (Table 2).

Later it will be seen that differences in the heat production between children of different nutritive condition are much greater than those represented by these specific gravities. It remains important, however, to obtain as much accurate information as possible on the heat produc-

13. Steinitz: Jahrb. f. Kinderh., 1904, lix, p. 447.

14. Steinitz and Weigert: Beitr. z. chem. Physiol. u. Path. (Hofmeister's), 1905, vi, 205.

tion of different types and to consider the value of the unit of weight as contrasted with the unit of surface. Comparisons will be made with the results found by all authors who have used methods at all comparable with ours.

The methods employed in this series of observations will be considered briefly, after which the results and their significance will be taken up.

TABLE 2.—METHOD OF CALCULATING SPECIFIC GRAVITY FROM DATA IN TABLE 1

| | Per Cent. | Specific Gravity | | |
|------------------------------|-----------|------------------|---|----------------|
| Atrophic child— | | | | |
| Water | 80 | 1.00 | = | 80 |
| Fat | 1.73 | 0.9 * | = | 1.557 |
| Ash | 3.00 | 2.25† | = | 6.75 |
| Protein and extractives..... | 14.6 | 1.5 ‡ | = | 21.90 |
| | | | | 1.0020 Sp. Gr. |
| Normal child— | | | | |
| Water | 70.15 | 1.00 | = | 70.15 |
| Fat | 13.11 | 0.9 | = | 11.799 |
| Ash | 2.73 | 2.25 | = | 6.143 |
| Protein and extractives..... | 14.01 | 1.5 | = | 21.015 |
| | | | | 1.0010 Sp. Gr. |
| Fat child— | | | | |
| Water | 58.94 | 1.00 | = | 58.94 |
| Fat | 24.17 | 0.9 | = | 21.753 |
| Ash | 2.98 | 2.25 | = | 6.705 |
| Protein and extractives..... | 13.91 | 1.5 | = | 20.865 |
| | | | | 1.0826 Sp. Gr. |

* Biochem. Handlexicon, 1911, iii, 175.

† Pfaunder: Ztschr. f. Kinderh., 1912, iii, 413.

‡ Estimated.

AUTHORS' EXPERIMENTS

The apparatus described by Murlin¹⁵ was used in this series of observations. Through the courtesy of Dr. L. E. La Fetra, chief visiting physician to the children's service, and of the hospital authorities, it was set up in the laboratory off the children's ward, and special connections to the water and electric supplies of the building were provided. We wish to express at this point our very great obligation to Dr. La Fetra for his unfailing helpfulness and encouragement. While the work is such as properly to require the attention of a special nurse and the subjects to be used should ideally be cared for in a special room or ward, through the hearty cooperation of the house physician, Dr. L. C. Schroeder and the head nurse, Miss Hein, very little inconvenience was experienced in obtaining subjects wanted at the proper time or in the proper condition as to food, sleep, etc. Our hearty thanks to these persons, as also to Dr. B. Kramer, who assisted in the last few weeks of the work, are due, and are here gratefully recorded.

15. Murlin: AM. JOUR. DIS. CHILD., January, 1915, p. 43.

The daily routine, while varied to suit the convenience of the observers, who were ourselves, was usually as follows: The water and power were turned on the incubator at about 9:30 a. m. By 10:30, as a rule, temperature conditions inside the incubator, even in the coldest weather, were perfectly stable and constant. The child selected, having been kept awake since the early morning feeding at 5 or 6 a. m., was brought to the laboratory at about this time. He was there first weighed stripped, immediately after this was immersed for the volume determination,¹² and as soon as clothed again was given food just before entering the incubator. The first period could as a rule be started within from fifteen minutes to half an hour after sealing up the inner chamber. On this schedule the respiratory observations were completed by about 1 p. m. Rarely an experiment was conducted in the afternoon also.

METHODS

1. *Heat Production.*—It was determined at the outset to make the measurement of the respiratory exchange as accurate as possible and to take into account the nitrogen of the urine, so that no factor should be lacking in the exact estimation of the heat production, which was calculated by the method of Zuntz and Schumburg.¹⁶ The exact determination of the oxygen absorption even from a chamber of small dimensions such as the one here employed, can be made only by analyzing the air at the beginning and end of each respiratory period. For example, if the child should void urine during the course of the period, the water vapor in the air immediately would rise very considerably, and if he should cry actively for as much as ten minutes, both the water vapor and the carbon dioxid would rise very perceptibly, thereby excluding some oxygen, which is fed in according to the air tension, and diminishing the apparent absorption. Many instances of this sort could be given from this series of experiments in which the respiratory quotient would have been many points below or above the actual value if this correction for the composition of the air had not been made. The conditions obtaining in an alcohol check experiment even where the same amount of oxygen is used up as in the experiment with the child, are not at all controlling; for in this case the amount of carbon dioxid and water vapor is very constant, and residual analyses are not so important, although they have in these experiments always been made. In view of the fact that Benedict and Talbot have

16. Zuntz and Schumburg: Studien zu einer Physiologie des Menschen, Berlin, 1901. See also Williams, Riche and Lusk: Jour. Biol. Chem., 1912, xii, 349.

made all of their heat calculations on the basis of the carbon dioxide instead of the oxygen, it should be noted that a much greater error¹⁷ is involved in this method when the respiratory quotient is not known exactly for the period under consideration than when the oxygen is used as the basis. Corrections were made also for temperature and barometric changes for each and every period of the experiments.

2. *Collection of Urine.*—The collection of urine in twenty-four-hour periods was accomplished successfully, though not without some difficulty, even with the female child. With Children 4 and 6 (Table 4), it may be seen how the total nitrogen in the urine varies but little from day to day so long as the food is constant, as to both quantity and quality, while with Child 3 may be seen the effect of varying the quality of the food. Since in all of these cases the food was purposely kept as nearly constant as possible, having regard for the welfare of the child, the urine was not collected for every experimental day, and in several instances was preserved for analysis on one day only.

The bed or frame used in the collection of the urine was one similar to that described by Hoobler,¹⁸ but small enough to be admitted to the inner chamber (Fig. 1). When urine was being collected for the twenty-four hours of which the experimental period was a part, the urine bottle was placed in the chamber with the child. When urine was not wanted for the period the child was provided with a double diaper to prevent vaporization as much as possible.

3. *Uniform Conditions.*—For the purpose of this investigation it was essential that the factors of food, muscular work and environing temperature should be as nearly constant for each individual as possible and should be comparable for different individuals. In some respects the conditions of inanition adopted by Schlossmann and Murschauser and Howland for the determination of the basal metabolism would have been more nearly ideal for the purpose. Judging by the difficulties experienced by Schlossmann and Murschauser in getting complete muscular rest, however, and with the feeling that the matter of muscular rest was much more important than the dynamic action of food, it was deemed best to feed the child as much as necessary to obtain, if possible, two continuous hours of sleep. It may be seen from Table 5 that in many instances there were two successive hours of sleep. More often the sleep terminated some time during the second

17. See e. g. A. Loewy: Oppenheimer's *Handbuch der Biochemie*, iv, p. 278, for the differences in heat value of a liter of oxygen and carbon dioxide. For a detailed discussion of this matter Cf. DuBois and Geppart, *Arch. Int. Med.*, to appear soon.

18. Hoobler: *AM. JOUR. DIS. CHILD.*, 1912, iii, 253.

period, or, if it did continue throughout the second, was less quiet than the first.

4. *Records of Movements.*—In order to secure the advantage of darkness in keeping the children asleep, a blanket was suspended across the glass front of the incubator as soon as the respiration chamber was closed. This made it impossible to see the motions of the subject. Furthermore, it was desired to make observations as to the relation between the pulse and respiration rates and the heat production, and to rule out the personal equation in making the enumeration of these movements. A means was devised, therefore, for recording both the pulse and the respiratory movements on a smoked paper.

A. *Pulse:* A small cuff such as is used in making blood-pressure determinations in the infant¹⁹ was placed about the left thigh. From this a rigid-walled tube was led to a glass connection passing through the wall of the incubator, thence to a T-tube on top of the incubator, one limb of which passed to a small air-pump and the other to a second T-tube. To the second T a mercury manometer was connected by one limb and a pressure-reducing bottle by the other (Fig. 1). From the pressure-reducing bottle, finally, a transmission tube led to a recording tambour covered with a piece of very thin rubber membrane. A pressure of from 30 to 40 mm. of mercury was found to be sufficient to give a legible motion to the lever, and it was found that this pressure did not interfere either with the circulation or with the repose of the child. After several trials it was found that two very thin finger-cots placed one inside the other sufficed to reduce the pressure in the pressure bottle and at the same time to transmit a sufficient wave to the tambour for a legible record on smoked paper.

Two kymographs of the Sherrington type were arranged as a long paper kymograph on top of the incubator. One complete revolution of this paper could be made to coincide with an hour's observations. The pulse naturally was not recorded legibly when the leg was being moved, although, as may be seen in Figures 5 and 6, it was often possible to count the pulsations even while the child was crying. Before the graphic method had been satisfactorily worked out the pulse with Child 1 was for a few days (Table 5) counted by means of the stethoscope. The only objection to this graphic method of counting the pulse which was encountered was the labor of enumerating the pulse waves of the record. Because of this, with the last three children the stethoscope was again used.

19. Hoobler: *Med. Rec.*, New York, December, 1911.

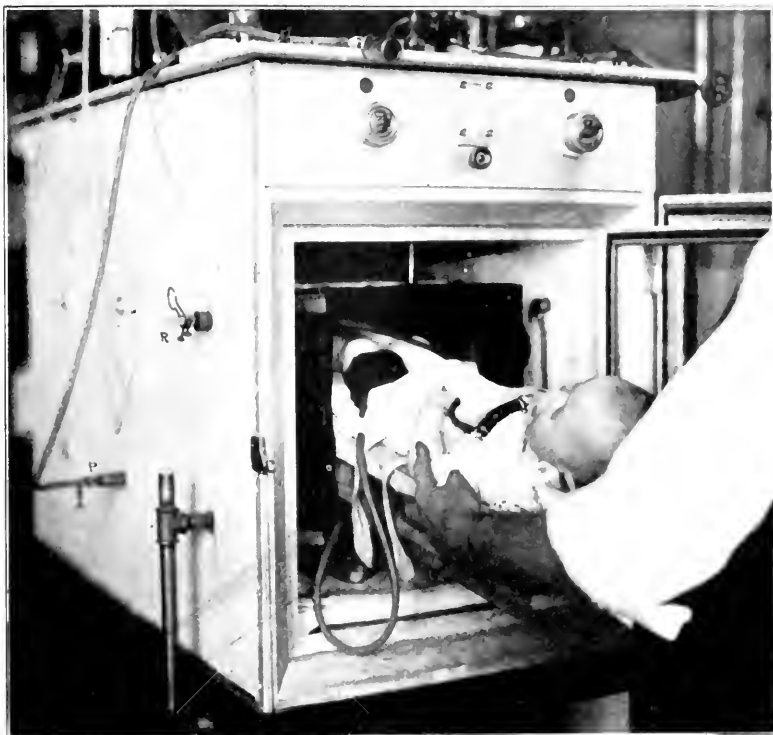


Fig. 1.—Showing arrangement of small cuff on the leg of infant for recording pulse, and small pneumograph around chest for recording respirations. The rubber tubing connecting with the tambours on top of the incubator are seen penetrating the outside wall. *P*, tubing for pulse; *R*, tubing for respiration.

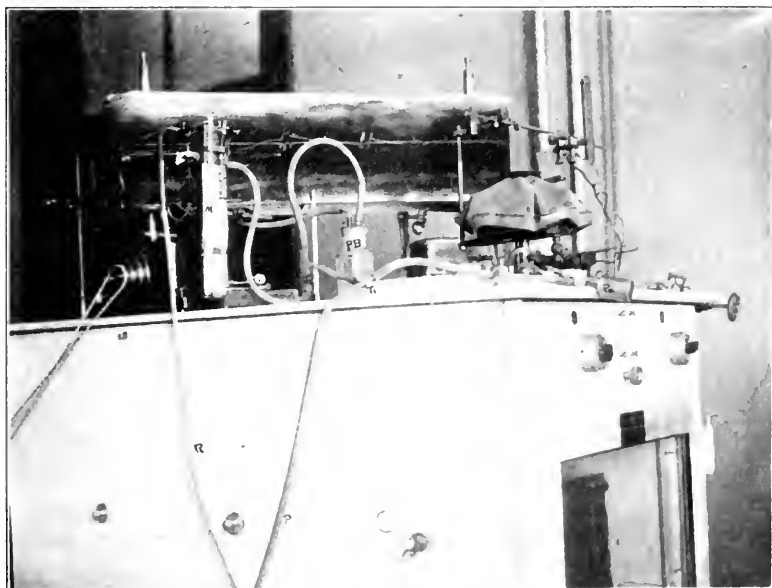


Fig. 2.—Showing arrangement of recording devices on top of the incubator. The tube *P* connects a T tube (1) with the hand pump and (2) with another T, which in turn connects with the mercury manometer *M*, and the pressure reducing bottle *PB*. From the pressure-reducing bottle a final tube leads to the recording tambour.

B. Respiration: For recording the respiratory movements and, incidentally, movements of the body and arms, a very short pneumograph of the type made by the Harvard Apparatus Company was used. The rubber tubing ordinarily used on these pneumographs not being sufficiently distensible for the baby's chest, it was replaced by a tube made from the finger of a surgeon's rubber glove. The one tube served throughout the entire series of observations.

C. Time: A record of the time in seconds was obtained simultaneously with the pulse and respiration by means of a Jacquet time recorder.

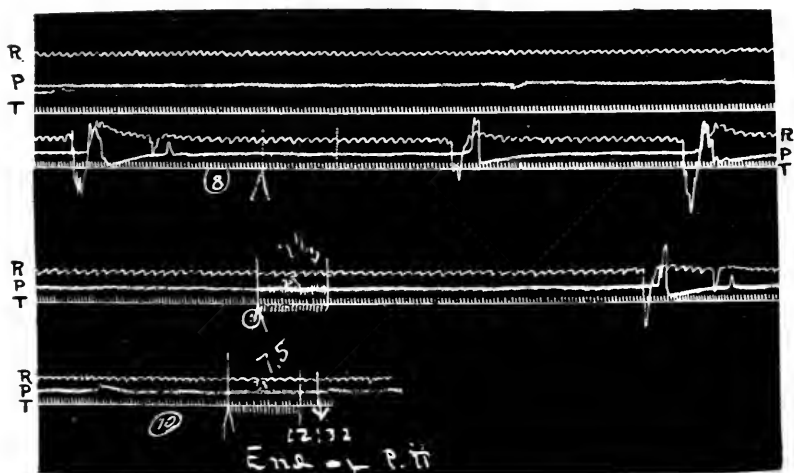


Fig. 3.—Sample from record for C. P., March 7. In this and the following figures upper tracing of each group *R* represents the respirations; the middle one, *P*, the pulse, and the lower one, *T*, the time in seconds. The record shows several readjustment movements, and the method of counting the pulse and respirations by drawing parallel lines twenty seconds apart perpendicular to the time record as base line.

Samples of the tracings secured by these methods are shown in Figures 3, 4, 5 and 6. With every child but one (C. M.) at least one complete hourly period as quiet as those shown in Figures 3 and 4 was obtained. Experience soon taught that when a child did not sleep soon after feeding it was time wasted to prolong the observation. In only the one case above mentioned, therefore, was the child permitted to indulge in prolonged crying. Naturally it was not difficult to tell at once when a child fell asleep. The perfectly regular respiration for two minutes or more could mean nothing else and even when the respirations were not perfectly regular the absence of larger spikes denoting continuous or frequent grosser movements always made this point perfectly certain. From these tracings, except in the instances

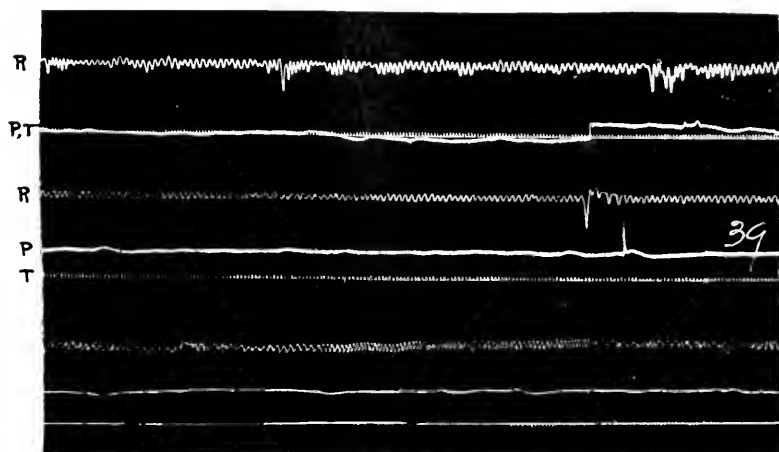


Fig. 4.—Sample from record for W. L., March 25, sleeping throughout. Three turns about the kymograph are intercepted. The respiration record shows type of irregular respirations (Cheyne-Stokes) referred to in Table 5.

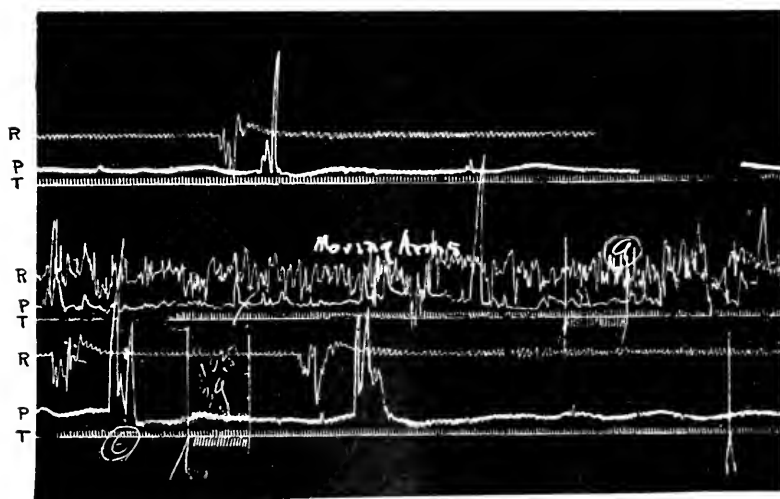


Fig. 5.—Sample from record for E. N., March 28, showing the character of the tracings obtained with a moderate degree of restlessness.

noted in the footnotes, were obtained the data given in Table 5 regarding muscular activity, pulse and respiration.

The Cheyne-Stokes type of respiration is common in these children. Sometimes a perfectly regular respiration wave would prevail through one period of the experiment and in the next the predominate form would be the Cheyne-Stokes. It was impossible to correlate its occurrence in any definite way with events in the alimentary system.

It is a perfectly familiar fact that a child even when perfectly healthy will not lie absolutely still for long at a time even in the most profound sleep. Now and then a sensory irritation from some part of the body will cause a series of movements which for convenience have been designated "readjustment movements." Figure 3 shows what is meant by this term. They occur in almost every record of the sleeping child, but recurred most frequently in the case of Child 4 on the third day of the protein milk formula.

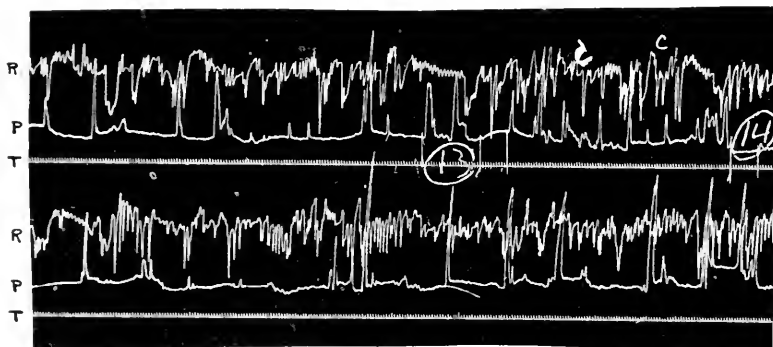


Fig. 6.—Sample from record for J. S., March 23, showing the character of tracings obtained with continuous restlessness and crying. At C and C the child was heard to cry out. The record shows that it is often possible to count the pulse even while the child is crying.

When the child waked after a sleeping period of an hour or two it did not lie still long. Rarely it would fall asleep again. Most commonly fretting or crying soon began and continued to the end of the period. The motions produced were unmistakable. Crying could also be heard even when the stethoscope was not used, by listening near the rubber bag used as a tension equalizer (Fig. 2). Table 5 exhibits in a number of instances the influence of crying a definite number of minutes in contrast with a perfect sleeping period.

5. *Temperature of the Incubator.*—The temperature shown in Table 4 represents the average temperature at the beginning and end of each period, respectively, as shown by two thermometers, one in

the inner chamber and one in the outer.²⁰ The temperature of the copper wall of the box, and hence of the air exposed to it inside, obviously was determined quite as much by the outside temperature as by the temperature of the air inside just above the child. From many experiments with alcohol checks it was learned that the average of the two thermometers gave a more accurate index than the average of all four thermometers. As may be seen from Table 4 this average temperature never fell below 27 and rarely rose above 29 C. The child on the bed was clothed with only a single garment, a knit or flannel shirt, or wrapper, and it was found that this temperature was most conducive to quiet sleep. Only when the child cried actively for several minutes did it perspire. Except in very few periods the temperature did not vary more than a half degree throughout the hour.

SUBJECTS OF EXPERIMENTS

CHILD 1.—W. So., admitted to Bellevue Hospital, pediatric division, Jan. 23, 1914, aged 1 year. The child was a perfectly well boy; he had never been ill and was brought to the hospital because his mother was about to be confined in the School for Midwifery and there was no one at home to take care of him. Physical examination was negative throughout. He weighed 21 pounds and 8 ounces on admittance. March 9 he was discharged from the hospital in care of his mother. While in the hospital the child took his feedings well, did not vomit, and the stools were normal.

CHILD 2.—A. Sa., admitted to Bellevue Hospital Feb. 9, 1914, aged 7 weeks. The child was a perfectly normal, healthy boy and was brought into the hospital because the mother was to undergo operation. The physical examination was negative throughout. While in hospital the child was fed partly on breast-milk and partly on diluted cow's milk. The child did not vomit; took feedings well; stools normal.

CHILD 3.—C. P., admitted to Bellevue Hospital Dec. 21, 1913, aged 1 month. Chief complaint was that of diarrhea and vomiting. Two weeks previous to admission the child was taken from the breast. Shortly thereafter he began to have loose, green stools, at first five to six daily; on admission two to three a day. During the three days before admission child had been vomiting four to six times daily after the cow's milk feeding. He cried almost constantly. Weight on admission 4 pounds and 3 ounces. Physical examination showed emaciated infant; eyes, cheeks and anterior fontanelle sunken. Child was put in premature room and fed on breast-milk and gradually increased in weight to 5 pounds and 9 ounces; stools became normal; vomiting ceased. Metabolism studied at this period. Died one week later.

CHILD 4.—E. N., aged 3 months, brought into Bellevue Hospital, pediatric division, because mother was undergoing an operation in Ward 16. Father had tried to care for child at home but when he cried a great deal (because of over feeding) and began to vomit, father brought him to hospital. Physical examination showed child to be a perfectly normal male, fairly well nourished, without the appearance of being sick. When placed on proper cow's milk dilutions vomiting ceased, stools were normal and child was in good condition at time metabolism studies were undertaken.

CHILD 5.—J. Sm., admitted to Bellevue Hospital, pediatric division, Feb. 22, 1914, 11 months of age, weight 11 pounds and 10 ounces. Child was brought

20. AM. JOUR. DIS. CHILD., January, 1915, p. 43.

into the hospital as a well baby, the mother being in the gynecological ward for an operation. Was only moderately nourished child, but physical examination showed no pathologic conditions except a discharging ear. At the time the metabolism studies were made child was taking feedings well; stools were normal; no vomiting.

CHILD 6.—W. L., aged 2 months; was deserted by mother after having been left in hospital. Child was perfectly normal, taking its feedings well; stools normal and no vomiting.

CHILD 7.—C. Ma., a breast-fed girl baby, 10 months old on March 10, 1914, was brought into pediatric division, Bellevue Hospital, while mother was undergoing an operation in gynecologic ward of same hospital. The child was a fat, healthy baby at the time metabolism studies were undertaken.

CHILD 8.—C. D., an undernourished white boy, admitted May 13, 1914, aged 3 months, was brought to hospital for regulation of its diet; had been fed on breast until two weeks before admission. Since then he has been fed on diluted cow's milk; vomited and had green stools. On proper diet vomiting ceased. Stools became normal and child was discharged to its mother June 23 in excellent condition.

TABLE 3.—SUMMARY OF DATA DESCRIBING SUBJECTS

| Name | Age, mos. | Weight, gm. | Sex* | Characterization of Condition |
|-------------|-----------|-------------|------|---|
| E. H. | 2½ | 4,690 | ♂ | Normal baby, average weight. |
| A. Sa. | 2 | 5,810 | ♂ | Perfectly healthy baby, considerably overweight. |
| W. L. | 2 | 4,364 | ♂ | Normal baby, near average weight. |
| F. N. | 3 | 4,115 | ♂ | A healthy child. His underweight only temporary, due to wrong diet shortly before entering hosp. |
| C. P. | 3 | 2,462 | ♂ | A markedly atrophic child in last stage of marasmus. |
| C. D. | 4 | 3,375 | ♂ | Considerably undernourished, and underweight. Disturbance of nutrition only. |
| M. Me. | 5¾ | 6,470 | ♂ | A child whose nutrition appeared entirely normal, but who no doubt had an incipient tuberculous infection. Normal weight. |
| C. Ma. | 10½ | 9,465 | ♀ | A healthy child considerably above the average weight due to excess of fatty tissue. |
| W. So. | 11-12 | 9,373 | ♂ | Healthy child, normal weight. |
| J. Sm. | 12 | 5,802 | ♂ | Much underweight. No proof of a diseased condition though suspected of hyperthyroidism after observations on metabolism. |

* In this column ♂ stands for male and ♀ for female.

CHILD 9.—E. H. (foundling), brought in by messenger June 16, 1914, was a healthy boy about 8 weeks of age with no physical abnormalities. While in hospital child gained in weight; stools were normal. On July 2 he was transferred to Foundling Hospital as a normal healthy baby.

CHILD 10.—M. Me., admitted to hospital on June 7, 1914, aged 5 months. Mother in hospital very ill with tuberculosis; subsequently died. Child showed positive von Pirquet; Roentgen-ray revealed no enlargement of bronchial lymph-nodes. Temperature 99.4 F. after experiment on June 30. July 1 temperature rose to 101.4 F. gradually subsiding, reaching normal July 4, otherwise temperature was within normal limits. The child was a well-developed boy with no evident signs of illness and when discharged appeared to be in good condition.

GROSS RESULTS

In presenting the results just as they came from the laboratory in chronologic order (Table 4), it may be stated at the start that in only five cases (one-half the total number reported) were the conditions of food, muscular repose, etc., what we would call *entirely* satisfactory. These can be readily picked out of the table by the fact of close agreement between the results *on successive days*. The ideal which was sought embraced the following experimental conditions: (1) the same food as regards quantity and quality on successive days for the same child; (2) approximately the same proportionate amount for different children; (3) the respiration experiment starting at nearly the same time after feeding on successive days, e. g., Child 4; (4) the child sleeping at least one full hour of the respiration period; (5) a uniform temperature. In the present state of our knowledge, conditions less rigid than these cannot meet the requirement of satisfactory proof or disproof of such a law as Rubner's law of surface area (see "Discussion" toward end of article).

The first and last of these conditions were the ones most easily fulfilled in our experiments and for evident reasons. The routine feedings of a given amount of food to well babies is readily accomplished with the help of well-trained nurses. The last feeding just before the respiration period was given by one of us and the amount taken (ounces on the nursing bottle) was noted. The calculation of the calories distribution in the food and the total amount in the last feedings is based on the average composition of the milk (and dextrimaltose) regularly used in the hospital.

As for giving the same proportionate amount of food to different babies, one is met at the outset with the dilemma of choosing a unit. Shall children be fed according to weight, surface area or age? In practice any of these standards must be constantly checked by observations as to the growth, digestion, etc., so that if a certain standard is selected (say 80 calories per kilogram per day or 10 calories per kilogram per feeding) conditions may arise necessitating a change, and this is very disconcerting to well-laid laboratory plans. Such difficulty at the very outset was met with in the case of Child 1 who developed a diarrhea on February 12 and the diet had, accordingly, to be changed. The same was true of Child 7.

The necessity for beginning the respiration experiment as nearly as possible the same length of time after the last feeding appeared early in the series. For example, with Child 1 (W. S.), February 10 and 11, when the experiments began twenty-three and twenty minutes, respectively, after feeding, the metabolism of the first hour (sleeping) was very nearly the same for the two days; while the next day when

TABLE 4 GROSS RESULTS OF METABOLISM FINDINGS OF TEN CHILDREN ARRANGED CHRONOLOGICALLY

| Date | Name and Age | Condition | Weight | Food Distribution of Calories in Per Cent. of Total | Last Feelings | | Respiration Period | CO ₂ Elim. L. | O ₂ Abs. L. | R. Q. | N In 24 Hour Urine | Temp. of Resp. Incubator | |
|------|-----------------------------|-----------------------|--------|---|---------------|-------------|--------------------|--------------------------|------------------------|-------|--------------------|--------------------------|------|
| | | | | | Amt. oz. | Time | | | | | | B. | E. |
| 2/1 | Child 1, W. So., 11-12 mos. | Normal boy | 9,290 | P21;F4;CH28.3 | 8 | A. M. 9:00 | 11:01-12:05 | 5,724 | 7,130 | 0.80 | | 29.5 | 29.6 |
| 2/6 | | | 9,179 | " " | 8 | P. M. 2:15 | 2:35-3:35 | 4,540 | 5,573 | 0.81 | 4,130 | 27.6 | 27.7 |
| 2/10 | | | 9,373 | " " | 8 | A. M. 10:30 | 10:43-11:43 | 4,122 | 5,011 | 0.82 | 4,298 | 27.6 | 28.0 |
| 2/11 | | | 9,440 | " " | 8 | 11:00 | 11:13-12:44 | 4,803 | 5,611 | 0.85 | | 26.45 | 28.1 |
| 2/12 | | | 9,215 | Formula P15;F23.6;CH31.4 | 10 | 11:00 | 11:20-12:20 | 4,345 | 4,929 | 0.88 | | 28.0 | 28.5 |
| 2/28 | | | 9,555 | Formula P15;F23.6;CH31.4 | 10 | 11:00 | 12:30-1:21 | 4,534 | 5,415 | 0.83 | | 28.5 | 28.8 |
| | | | | Formula P15;F23.6;CH31.4 | 10 | 11:00 | 12:15-1:15 | 4,411 | 5,526 | 0.79 | 3,948 | 28.3 | 28.3 |
| | | | | Formula P22;F30;CH28 | 10 | 9:00 | 11:15-2:15 | 5,021 | 5,872 | 0.85 | | 28.3 | 29.4 |
| | | | | | 8 | 10:45 | 11:16-12:16 | 4,970 | 5,489 | 0.90 | | 28.7 | 28.8 |
| | | | | | 8 | 10:45 | 12:16-12:56 | 3,445 | 2,791 | 0.91 | | 28.8 | 28.7 |
| 2/13 | Child 2, A. Sa., 2 months | Normal boy overweight | 5,890 | At breast | ? | 10:30 | 12:52-1:32 | 1,545 | 1,811 | 0.85 | | 29.7 | 30.3 |
| 2/14 | | | 5,810 | Form. P10;F22.5;CH67.5 | 3 | 9:00 | 12:22-1:13 | 1,871 | 2,070 | 0.90 | 0,658 | 30.3 | 30.2 |
| 2/16 | | | 5,692 | Mother's Milk | 2 | 11:00 | 1:13-2:04 | 2,406 | 2,700 | 0.89 | | 30.2 | 30.4 |
| 2/17 | | | 5,690 | Mother's milk | 3 | 9:00 | 10:29-11:31 | 2,164 | 2,509 | 0.86 | 0.812 | 28.4 | 28.6 |
| | | | | Formula P12;F20;CH167 | 3 | 10:30 | 11:31-12:38 | 4,050 | 3,859 | 1.04 | | 28.6 | 28.5 |
| | | | | | 3 | 10:30 | 11:27-12:27 | 2,301 | 3,051 | 0.75 | | 27.4 | 27.5 |
| | | | | | 3 | 10:45 | 12:27-1:27 | 2,581 | 2,914 | 0.88 | | 27.5 | 28.3 |
| 2/27 | Child 3, C. P., 3 months | Atrophic | 2,462 | Formula P11;F25;CH64 | 3 | 9:00 | 11:48-12:48 | 1,570 | 1,448 | 1.08 | | 28.1 | 28.4 |
| 3/3 | | | 2,515 | " " | 3 | 10:45 | 12:48-1:48 | 1,430 | 1,429 | 1.00 | | 28.4 | 28.7 |
| | | | | Formula P11;F75;CH14 | 3 | 9:00 | 10:40-11:40 | 1,569 | 1,448 | 1.08 | 0.692 | 27.8 | 27.8 |
| | | | | | 1/2 | 10:30 | 11:40-12:40 | 1,369 | 1,499 | 0.91 | | 27.7 | 28.2 |
| 3/7 | | | 2,444 | Formula P11;F75;CH14 | 3 | 1:00 | 3:03-4:03 | 1,114 | 1,150 | 0.97 | 1,036 | 28.3 | 28.6 |
| 3/10 | | | 2,434 | Formula P29 C;F55.7;CH14.7 | 3 | 2:30 | 4:03-5:05 | 1,140 | 1,324 | 0.86 | | 28.6 | 28.9 |
| | | | | | 3 | A. M. 9:30 | 10:32-11:32 | 1,364 | 1,675 | 0.81 | 1,330 | 29.1 | 29.2 |
| | | | | | 3 | 9:30 | 11:32-12:32 | 1,282 | 1,778 | 0.72 | | 29.2 | 28.9 |
| 3/17 | Child 4, E. N., 3 months | Underweight | 4,115 | Formula P10;F24;CH66 | 3 | 9:00 | 11:10-12:10 | 2,154 | 2,188 | 0.98 | 1,120 | 28.6 | 29.0 |
| 3/18 | | | 4,134 | Formula P10;F24;CH66 | 3 | 10:30 | 12:10-1:10 | 1,968 | 2,208 | 0.89 | | 29.0 | 28.9 |
| 3/19 | | | 4,147 | " " | 3 | 9:00 | 11:10-12:10 | 2,295 | 2,072 | 1.11 | 1,092 | 28.5 | 28.1 |
| | | | | | 3 | 10:30 | 12:10-1:11 | 2,503 | 2,432 | 1.03 | | 29.1 | 29.7 |
| | | | | | 3 | 9:00 | 11:10-12:10 | 2,069 | 2,096 | 1.00 | 1,064 | 28.8 | 28.9 |

| | | | | | | | | | | | | | | | |
|------|----------------------------|---------------------------|-------|---------------------------|---|-------|-----|-------------|-------|-------|------|-------|-------|------|------|
| 3/21 | Child 5, J. Sm., 12 months | Underweight | 5,802 | Formula P22; F50; OH28 | 7 | 9:00 | 92 | 11:25-12:33 | 4,081 | 4,202 | 0.97 | 3,780 | 20.74 | 28.8 | 29.1 |
| 3/23 | | | 5,713 | " | 7 | 10:45 | 92 | 12:23-1:23 | 3,450 | 4,306 | 0.79 | | 20.59 | 29.1 | 28.8 |
| | | | | " | 7 | 9:00 | 92 | 11:00-12:00 | 3,557 | 4,076 | 0.87 | 2.91 | 19.78 | 29.0 | 29.2 |
| | | | | " | 7 | 10:45 | 92 | 12:00-1:00 | 4,104 | 4,477 | 0.92 | | 21.88 | 29.2 | 29.2 |
| 3/24 | Child 6, W. L., 2 months | Normal | 4,364 | Formula | 3 | 9:00 | 39 | 10:45-11:45 | 1,965 | 2,152 | 0.92 | 0.924 | 10.56 | 29.1 | 29.2 |
| 3/25 | | | 4,371 | P11; F25; OH64 | 3 | 10:10 | 39 | 11:45-12:45 | 2,416 | 2,673 | 0.90 | | 13.09 | 29.2 | 28.8 |
| 3/26 | | | 4,350 | Formula | 3 | 9:00 | 36 | 10:35-11:38 | 2,015 | 2,190 | 0.92 | 1.008 | 10.74 | 28.8 | 29.1 |
| | | | | P12; F27; OH61 | 3 | 10:15 | 36 | 11:35-12:38 | 2,036 | 2,266 | 0.87 | | 11.09 | 29.1 | 29.2 |
| | | | | " | 3 | 9:00 | 36 | 11:10-12:10 | 2,040 | 2,181 | 0.93 | 1.008 | 10.75 | 29.2 | 29.4 |
| | | | | " | 3 | 10:50 | 36 | 12:10-1:10 | 2,065 | 2,309 | 0.92 | | 11.31 | 29.4 | 29.5 |
| 3/24 | Child 7, C. Ma., 10½ mos. | Normal girl overweight | 9,382 | Whole milk | 8 | P. M. | 148 | 3:28-4:28 | 4,529 | 5,518 | 0.82 | 1.20 | 26.54 | 28.6 | 29.1 |
| 3/25 | | | 9,492 | P22; F50; OH28 | 9 | 3:00 | 37 | 3:28-4:13 | 8,821 | 3,934 | 0.71 | | 24.50 | 28.7 | 29.1 |
| 3/26 | | | 9,465 | Form. (dil. whole milk) | 8 | 3:00 | 92 | 4:13-4:58 | 3,013 | 3,819 | 0.78 | | 30.19 | 29.1 | 29.4 |
| | | | | P22; F50; OH28 | 2 | 3:00 | 23 | 3:41-4:26 | 3,471 | 4,846 | 0.72 | 1.052 | 30.18 | 28.8 | 29.5 |
| | | | | Whole milk | 8 | 1:00 | 148 | 4:26-5:11 | 3,230 | 4,246 | 0.76 | | 27.24 | 29.5 | 29.8 |
| | | | | P22; F50; OH28 | 2 | 3:10 | 37 | 5:11-6:11 | 3,363 | 5,162 | 0.70 | | 24.09 | 29.8 | 29.3 |
| 6/10 | Child 8, C. D., 4 months | Underweight boy | 3,510 | Formula | 4 | M. | 47 | 2:33-3:36 | 2,348 | 2,889 | 0.82 | | 13.16 | 28.1 | 27.1 |
| 6/11 | | | 3,375 | P16; F25; OH59 | 4 | P. M. | 47 | 3:36-4:36 | 2,699 | 2,726 | 0.99 | | 13.61 | 27.1 | 28.0 |
| 6/18 | | | 3,440 | " | 4 | M. | 47 | 3:30-4:30 | 1,861 | 1,861 | 1.00 | | 9.26 | 28.3 | 27.9 |
| | | | | " | 4 | P. M. | 47 | 4:30-5:25 | 2,314 | 2,185 | 1.06 | | 11.89 | 27.9 | 28.4 |
| | | | | " | 8 | M. | 35 | 2:39-3:39 | 1,786 | 2,207 | 0.79 | 0.896 | 10.79 | 27.1 | 27.8 |
| | | | | " | 8 | P. M. | 35 | 3:39-4:39 | 1,940 | 2,192 | 0.87 | | 10.67 | 27.8 | 27.9 |
| 6/24 | Child 9, F. H., 2½ mos. | Normal boy | 4,690 | Formula | 4 | M. | 58 | 4:00-5:00 | 2,460 | 2,548 | 0.96 | 0.924 | 12.68 | 28.0 | 28.3 |
| 6/26 | | | 4,637 | P13; F28; OH59 | 4 | P. M. | 58 | 5:00-6:00 | 2,468 | 2,635 | 0.92 | | 12.99 | 28.3 | 29.9 |
| | | | | " | 4 | M. | 58 | 2:46-3:46 | 2,217 | 2,528 | 0.88 | | 12.33 | 28.0 | 28.0 |
| | | | | " | 4 | P. M. | 58 | 3:46-4:46 | 2,261 | 2,579 | 0.89 | | 12.45 | 28.0 | 28.3 |
| 6/29 | Child 10, M. Me., 5¼ mos. | Positive von Pirquet | 6,470 | Formula | 6 | P. M. | 101 | 3:16-4:17 | 3,278 | 3,336 | 0.98 | 1.428 | 16.82 | 28.2 | 28.7 |
| | | Normal | 6,460 | P14; F30; OH56 | 6 | 2:50 | 101 | 4:17-5:17 | 3,150 | 3,912 | 0.93 | | 16.92 | 28.7 | 28.5 |
| | | weight | | " | 6 | 2:50 | 101 | 3:19-4:20 | 3,098 | 2,992 | 1.03 | | 14.54 | 28.2 | 28.8 |
| | | | | " | 6 | 2:50 | 101 | 4:20-5:20 | 3,150 | 3,912 | 0.81 | | 18.08 | 28.8 | 28.4 |

* Formula for this feeding was P25; F56; OH19.

the experiment was delayed to an hour and a quarter after feeding, the child woke fifteen minutes (Table 5) before the end of the first hour and, by restlessness, raised his metabolism more than 10 per cent.

From the respiratory quotient it would seem that in one case at least, Child 8 (C. D.), there must have been delayed absorption of the food. The earlier the first period started after the last feeding, the lower was the respiratory quotient; thus:

| | |
|-----------------------------|-------------|
| June 18, 12 minutes, | R. Q., .79 |
| June 10, 33 minutes, | R. Q., .82 |
| June 11, 1 hour 30 minutes, | R. Q., 1.00 |

The food throughout was the same in quality. Since absorption takes place from the stomach very slowly as compared with absorption from the intestine, the indications are that the delay took place at the pylorus. There were no clinical signs of a stenosis. The case seems, however, to illustrate the importance of meeting the same conditions of absorption on successive days. When such conditions are satisfactorily met (as, for example, with Children 1, 4, 6, etc.), one should get the same respiratory quotient in corresponding hours with the same child.

THE DYNAMIC EFFECT OF FOODS

Whether a diet of mother's milk or of cow's milk sufficient to maintain active growth in the child, exerts a dynamic action on the heat production is not yet clear from the published researches. Rubner and Heubner²² were of the opinion that they had demonstrated such an effect as regards cow's milk in their paper on the artificial nutrition of a normal and an atrophic infant. They estimated that a diet of cow's milk for the normal infant containing 44 per cent. more than the maintenance requirement raised the metabolism 9.7 per cent., while for the atrophic infant a diet containing 35.5 per cent. more than the requirement for maintenance raised the heat production 5.2 per cent. In a later paper²³ the same authors compared the metabolism of a breast-fed baby on full diet for four days with his metabolism on one day when he received only tea instead of the breast-milk. The metabolism on the day of starvation was even higher than the average of the four days on food. The experiment failed, therefore, to show any dynamic action of the food. This cannot be accepted as conclusive, however, for the reason that no graphic record of the child's activities was made. One would naturally expect a normal baby deprived of food to be more active than when well fed.

There can be scarcely any doubt that the child does respond to the dynamic action of the specific foodstuffs in much the same manner

²² Rubner and Heubner: *Ztschr. f. Biol.*, 1899, xxxviii, 315.

²³ Rubner and Heubner: *Ztschr. f. exper. Path. u. Therap.*, 1905, i, 1.

as an adult. Howland⁹ was able to demonstrate an increase in the heat production of 10 per cent. by addition of 15 gm. of nutrose (5 gm. to each of three feedings) containing 14.25 per cent. nitrogen, in a child 3 months of age and an increase of 26 per cent. by addition of 30 gm. nutrose in another 7 months of age. A similar effect of increasing fat in the food was observed by Niemann²⁴ on a normal, though at the time, underweight, child 4 weeks of age by means of the Voit-Pettenkofer apparatus. In one period of four days when the food contained 127 calories from protein, 105 from fat and 168 from carbohydrate, or 400 calories in all, the average daily metabolism was 521 calories, or 1,337 calories per square meter per day. In the following period of five days the food contained 145 calories from protein, 368 from fat and 177 from carbohydrate, or 629 calories in all. The heat production in this period averaged 569 calories per day or 1,443 calories per square meter per day. An increase of 70 per cent. in the energy intake (largely fat) increased the metabolism 10 per cent. Niemann²⁵ observed a similar effect of increasing the fat in the food of an atrophic child 22 weeks old. Bahrdr and Edelstein²⁶ report an unusually high metabolism in an atrophic child fed on half milk with the addition of 5 per cent. milk-sugar, and express the opinion that this result, in contrast with the results of Rubner and Heubner and Niemann on atrophic children, was due to the high carbohydrate feeding. As already stated above, caution must be exercised in accepting any of these results obtained without a record of the child's activity or with one child as compared with another; but there is an evident possibility from the results cited that each and all of the foodstuffs may exercise a distinct dynamic action.

Frank and Wolff²⁷ have, apparently, confirmed on an extremely atrophic infant of 4½ months the interesting observation, first made by Rubner, that protein retained does not exert any specific dynamic action. In a period of three days when the food contained 102 calories from protein, 162 from fat and 166 from carbohydrate, 1.032 gm. nitrogen were retained daily and the child produced 1,581 calories per square meter per day. In a subsequent period of four days when the food contained 97 calories from protein, 139 from fat and 193 from carbohydrate, the nitrogen retention was 1.358 gm. per day and the heat production only 1,431 calories per square meter (Meeh) per day. This has been confirmed by one of us (H.) in collaboration

24. Niemann: *Jahrb. f. Kinderh.*, 1911, lxxiv, 650.

25. Niemann: *Festschrift z. Heubner*, Berlin, 1913, p. 467.

26. Bahrdr and Edelstein: *Festschrift z. Heubner*, Berlin, 1913, p. 1.

27. Frank and Wolff: *Jahrb. f. Kinderh.*, 1913, lxxviii, *Ergänzungsheft*, p. 1.

with Professor Lusk on the child L. of this series (results will be reported separately).

Notwithstanding the signs of dynamic action in all of this work, it has been found by Schlossmann and Murschauser and also by Howland that complete deprivation of food for from eighteen hours⁹ to forty-eight hours²⁸ does not lower the heat production of the child. Schlossmann and Murschauser kept a graphic record made by an eyewitness of the activity of their subjects. Benedict and Talbot¹⁰ also assert that in some instances the heat production (based on carbon dioxide) in their subjects twenty-one hours after food was "greater, even in periods of complete muscular repose," than immediately after food. In others, however, they were able to note an increase soon after feeding of from 5 to 10 per cent. above the heat production obtained from eighteen to twenty-one hours after.

While the weight of evidence from all of the previous work, therefore, is that the dynamic action of a sufficient dietary to keep the child growing actively is not very considerable, the effort has been made in this work to maintain such influence as the food may exert at an even level. Table 4 shows the distribution of the calories to the different organic constituents and the total amount received by the child at the last feeding before the respiration period.

In none of the experiments recorded here is the influence of food contrasted with complete inanition. In at least two of these, however, the dynamic influence of a large feeding as contrasted with a small one is plainly evident. Thus, Child 1 on February 28, had for clinical reasons been on a modified protein milk and received at 9 o'clock 223 calories of such milk. This was followed at 10:45 with an extra feeding of whole milk containing 148 calories. The respiration period started at 11:16, forty-six minutes after the last feeding. The child slept throughout the first hour but produced 12 per cent. more heat than he did on February 10, the corresponding hour following a single feeding of 148 calories in whole milk at 10:30.

Similarly, Child 2, because he had not previously slept more than one hour in the respiration chamber, was, on February 17, given two of his usual feedings only fifteen minutes apart. This time he slept nearly through the second hourly period, but produced two and a half calories per hour more than he had produced on February 14, when the feedings were two hours apart, or on February 16, when only one feeding, the regular one at 9 a. m., was given.

Since the two cases just mentioned represent the widest variations in the influence of different quantities of food in these experiments,

²⁸ Schlossmann and Murschauser: *Biochem. Ztschr.*, 1913, lvi, 355, and lviii, 483; also Murschauser: *Boston Med. and Surg. Jour.*, 1914, clxxi, 185.

it is probable that the dynamic effect of the diets of the different subjects would not vary more than from 10 to 12 per cent.

With only one child (C. P.) was the food intentionally varied for the purpose of studying the effect of the change. After obtaining perfect duplicates on the high carbohydrate formula for two days, in the hope of benefiting his nutritive condition, he was placed for one day on a high fat formula (March 7). The result was a striking drop in the heat production. No clinical benefit appearing, he was next given a high protein formula for two days and on March 10 while still on this formula his metabolism was again studied. The nitrogen in the urine rose in response to the greater intake of protein and a significant rise in the heat production was found. The only difference in muscular activity in these periods was the greater number of the "readjustment movements" recorded on the "high protein" day (in Table 5). These brief and purely incidental results, so far as they go, are in accordance with the facts concerning the dynamic action of the foodstuffs in dogs established by Professor Lusk²⁹ and his co-workers in his (physiological) laboratory.

METABOLISM IN RELATION TO MUSCULAR ACTIVITY

Benedict and Talbot³⁰ as well as Schlossmann³¹ have properly emphasized recently the importance of recording as exactly as possible the degree of muscular activity in any study of the energy metabolism of infants. The experiments of this series have fulfilled this requirement fully. Examples of the graphic records obtained (see preceding description of methods, Figs. 1 and 2) are given in Figures 3 to 6.

In Table 5 is found a description of the child's condition of repose for each period. The abbreviation "r. m." or "read. mov." denotes the readjustment movements such as may be seen in Figure 3. When only these movements are mentioned it is to be understood that there are no others of any description visible on the records except the regular pulsations of the artery and the regular movements of the chest. Types of irregular respiration are seen in Figures 4 and 5.

RELATION OF METABOLISM TO PULSE-RATE

It is our belief that this relationship can easily be overestimated. Murlin and Greer³² have discussed this point fully and have attempted to analyze the factors involved, in a study of the relation of heart action to the respiratory metabolism of adult men and of anesthetized dogs. It was emphasized that the pulse-rate can be parallel to the respiratory

29. Jour. Biol. Chem., 1912, xii; several papers.

30. Benedict and Talbot: AM. JOUR. DIS. CHILD., 1912, iv, 129.

31. Schlossmann: AM. JOUR. DIS. CHILD., 1913, vi, 15.

32. Murlin and Greer: Am. Jour. Physiol., 1914, xxxiii, 253.

TABLE 5.—METABOLISM IN RELATION TO MUSCULAR ACTIVITY, PULSE AND RESPIRATION RATE.
ARRANGED ACCORDING TO AGE

| Date 1914 | Name and Age | Peri- od | Condition of Muscular Activity | Aver- age Pulse- Rate | Aver- age Resp. Rate | Calo- ries per Hour | At This Rate Total Cal. Pro- duced in 24 Hours | Total Cal. in Food in 24 Hrs. | At This Rate Per Cent. of Intake Con- sumed |
|--------------|------------------|-------------|---|--------------------------------|-------------------------------|------------------------------|---|--|--|
| 2 13 | A. S., 2 months | ... | Sleeping throughout; 8 read. mov. | 148 | 34 | 13.92 | 334 | 348 | 96 |
| 2 14 | | I | Sleeping throughout; 5 read. mov. | 133 | Not Rec. | 12.00 | 288 | 326 | 88 |
| | | II | Sleeping all but 10 minutes Sleeping throughout; 5 read. mov. | 147 | | 15.42 | 370 | ... | 114 |
| 2 16 | | I | Two read. mov.; cried 10 min. | 123 | 35 | 11.78 | 283 | 304 | 93 |
| | | II | Sleeping 21 min.; cried 40 min. | 141 | 33 | 17.45 | 415 | ... | 138 |
| 3 17 | E. N., 3 months | I | Sleeping throughout; 3 read. mov.; resp. irregular | 134 | 46 | 14.50 | 349 | 378 | 92 |
| | | II | Sleeping all but 15 minutes; cried four times | 135 | 51 | 14.20 | 341 | ... | 90 |
| 3 24 | W. L., 2 months | I | Sleeping throughout; 7 read. mov.; resp. irregular | 127 | 31 | 10.56 | 253 | 351 | 72 |
| | | II | Sleeping all but 18 min.; cried continuously 18 min. | 131 | 27 | 13.09 | 314 | ... | 89 |
| 3 25 | | I | Sleeping throughout; 7 read. mov.; resp. irregular | 118 | 29 | 10.74 | 258 | 324 | 80 |
| | | II | Sleeping all but 2 min.; cried just at end; 6 read. mov. | 120 | 33 | 11.09 | 266 | ... | 82 |
| 3 26 | | I | Sleeping all but 1 min.; cried; resp. irregular | 118 | 28 | 10.75 | 258 | 324 | 80 |
| | | II | Sleeping all but 4 min.; cried several times; resp. irregular | 117 | 33 | 11.31 | 271 | ... | 84 |
| 2 24 | E. H., 2½ months | I | Moving (arms only) one-third of time; slept entire time | 135* | 42 | 12.68 | 304 | 409 | 74 |
| | | II | Slept entire time; restless ½ of hour | 133 | 38.4 | 12.99 | 312 | 409 | 76 |
| 2 26 | | I | Slept entire time; moving 3 min.; 4 read. mov. | 131 | 41 | 12.23 | 294 | 409 | 72 |
| | | II | Slept entire time; 8 read. mov. | 127 | 37 | 12.45 | 299 | 409 | 73 |
| 3 17 | E. N., 3 months | I | Sleeping throughout; 5 read. mov. | 112 | 25 | 10.87 | 261 | 337 | 77 |
| | | II | Sleeping throughout; 3 read. mov. | 110 | 26 | 10.75 | 258 | ... | 76 |
| 3 18 | | I | Sleeping all but 10 min.; rest- less those 10 min. | 122 | 39 | 10.53 | 292 | 337 | 75 |
| | | II | Sleeping 40 min.; fretted and cried 20 min. | 126 | 34 | 12.04 | 289 | ... | 86 |
| 3 19 | | I | Sleeping throughout; 8 read. mov. | 115 | 29 | 10.47 | 251 | 337 | 75 |
| | | II | Cried almost all the time | 127 | 41 | Leak | | | |
| 2 27 | C. P., 3 months | I | Sleeping throughout; 8 read. mov.; 8 long breaths | 122 | 28 | 7.35 | 176 | 307 | 57 |
| | | II | Sleeping throughout; 4 read. mov.; 10 long breaths | 130 | 27 | 7.15 | 171 | ... | 56 |
| 3 3 | | I | Sleeping throughout; 10 read. mov.; 5 long breaths | † | 27 | 7.35 | 176 | 304 | 58 |
| | | II | Sleeping throughout; 15 read. mov.; 4 long breaths | | 26 | 7.43 | 178 | ... | 59 |
| 3 7 | | I | Sleeping throughout; 6 read. mov.; 5 long breaths | 96 | 22 | 5.65 | 135 | 308 | 44 |
| | | II | Sleeping all but 2 min.; cried near end | 99 | 21 | 6.37 | 153 | ... | 50 |
| 3 10 | | I | Sleeping throughout; 20 read. mov. | 110 | 32 | 7.97 | 191 | 319 | 60 |
| | | II | Sleeping throughout; 35 read. mov. | 110 | 29 | 8.27 | 198 | ... | 62 |

* Pulse counted by stethoscope every five minutes.

† Pulse could not be counted.

TABLE 5.--(Continued)

| Date 1914 | Name and Age | Period | Condition of Muscular Activity | Average Pulse-Rate | Average Resp. Rate | Calories per Hour | At This Rate Total Cal. Produced in 24 Hours | Total Cal. in Food in 24 Hrs. | At This Rate Per Cent of Intake Consumed |
|-----------|--------------------|--------|---|--------------------|--------------------|-------------------|--|-------------------------------|--|
| 6/10 | C. D., 4 months | I | Moving all but 10 minutes | No Rec-ord | 30.7 | 13.16 | 306 | 328 | 93 |
| | | II | Sleeping 39 min.; awake, playing, crying, fretting 21 min. | No Rec-ord | 27.2 | 13.61 | 326 | ... | 100 |
| 6/11 | | I | Slept perfectly all through | No Rec-ord | 24.5 | 9.26 | 222 | 328 | 68 |
| | | II | Moving all but 10 min.; crying toward end | No Rec-ord | ? | 11.89 | 285 | ... | 87 |
| 6/18 | | I | Slept entire time; 10 read. mov. | 103* | 30 | 10.79 | 258 | 328 | 79 |
| | | II | Slept entire time; slightly restless | 99 | 25.8 | 10.67 | 256 | ... | 79 |
| 2/29 | M. Me., 5¼ mos. | I | Slept entire time; 5 read. mov. | 143* | 39 | 16.32 | 392 | 605 | 64 |
| | | II | Slept entire time; moving 4 min. | 139 | 40 | 16.92 | 406 | 605 | 67 |
| 2/30 | | I | Slept entire time; 3 read. mov. | 138 | 39 | 14.54 | 349 | 605 | 57 |
| | | II | Slept entire time; 14 read. mov. | 137 | 41 | 18.68 | 448 | 605 | 74 |
| 3/24 | C. Ma., 10 months | I | Sleeping only 15 min.; moving hands--crying | 118 | 46 | 26.54 | 637 | 775 | 82 |
| 3/25 | | I | Sleeping only 10 min.; playing with hands and crying occasionally for 35 min. | 114 | 41 | 24.50 | 588 | 555 | 106 |
| | | II | About same as P. I. | 122 | 40 | 24.19 | 580 | ... | 104 |
| 3/26 | | I | Sleeping only 10 min.; playing with hands; cried hard at end | 124 | 42 | 30.18 | 724 | 777 | 93 |
| | | II | Restless entire period; cried occasionally | 128 | 43 | 27.24 | 654 | ... | 84 |
| | | III | Lying still, playing with hands 15 min.; sleeping 45 min. | 117 | 32 | 24.09 | 578 | ... | 74 |
| 2/ 6 | W. So., 11-12 mos. | I | Sleeping all but 5 minutes | † | | 26.50 | 636 | 770 | 83 |
| 2/10 | | I | Sleeping throughout..... | 112‡ | | 23.88 | 573 | 770 | 74 |
| | | II | Sleeping 28 min.; awake but not crying 32 min. | ? | | 26.45 | 635 | ... | 82 |
| 2/11 | | I | Sleeping throughout..... | 115‡ | | 23.51 | 564 | 770 | 73 |
| | | II | Sleeping throughout, but restless most of period | 122‡ | | 25.43 | 610 | ... | 79 |
| 2/12 | | I | Sleeping all but 15 min.; restless than 15 min. | 123 | 42 | 26.23 | 629 | 450 | 140 |
| | | II | Sleeping only 10 min.; restless, but not crying, 50 min. | 132 | 51 | 28.25 | 678 | ... | 151 |
| 2/28 | | I | Sleeping throughout; 6 read. mov.; resp. irregular | 128 | 43 | 26.72 | 641 | 815 | 79 |
| | | II | Sleeping throughout but restlessly; 9 read. mov.; resp. irregular | No Rec-ord | 48 | 27.75 | 667 | ... | 82 |
| 3/21 | J. Sm., 1 year | I | Restless and fretting more than two-thirds of period | 118 | 41 | 20.74 | 498 | 462 | 108 |
| | | II | Sleeping all but 2 min. at beg.; 4 read. mov. | 112 | 38 | 20.59 | 494 | ... | 107 |
| 3/23 | | I | Sleeping all but 10 min.; cried few times | 112 | 36 | 19.78 | 474 | 481 | 99 |
| | | II | Fretted entire period..... | 126 | 40 | 21.88 | 525 | ... | 109 |

* Pulse counted by stethoscope every five minutes.

† Pulse could not be counted.

‡ Pith ball in blood-pressure app.

metabolism and the heat production only in case the volume output of the heart in different degrees of activity remains the same and the utilization of oxygen from the blood per heart-beat is the same. The same principles must obviously apply to the circulatory system of the child. Even in moderate degrees of activity produced by lifting a weight it was found in the work just cited that the product of the pulse-pressure³³ by the pulse-rate is a better criterion of the metabolism than is the pulse-rate alone.

That in greater variations of muscular activity the parallelism between pulse-rate and heat production does not hold for adults has been conclusively proven by Benedict and Cathcart³⁴ and more recently by Henderson and Prince.³⁵ Markwalder and Starling³⁶ using the heart-lung preparation of the dog have shown that when the pulse-rate is changed, e. g., from 72 to 156, the pulse-volume changes reciprocally, e. g., from 9.05 to 4.16 c.c. The total minute volume of blood-flow, however, remained the same.

With the same individual under the same conditions of food, temperature, etc., one would expect that minor fluctuations in muscular activity would be accompanied by fluctuations in the pulse-rate in the same direction, and this is borne out by a study of Table 5. As between children of different ages, where the pulse-rate for quiet sleep falls from 140 for a child of 2 months to 112 for a child of 12 months (Table 5), while the heat production nearly doubles, it is evident that the pulse-rate can be no criterion of metabolism.

The case of C. P. suggests the possibility of a relationship between the kind of food and the pulse-rate. This case has already been considered in connection with the dynamic action of the food. It may be seen from Table 5 that this child had a higher pulse-rate on a high carbohydrate food than on the high protein food which produced a greater dynamic action; while on the high fat formula both the pulse and metabolism were low.

The fourth column of Table 5 shows what the total metabolism in twenty-four hours would be if the same conditions of muscular activity, food, etc., continued for that length of time. It must be borne in mind that this way of expressing the metabolism is of doubtful value from the practical side and is adopted in this paper simply to serve as a basis of comparison between the results of this investigation and those of others. The plan adopted by Carpenter and

33. It was deemed impracticable in these experiments to obtain accurate readings of the pulse-pressure because of the risk of waking the child.

34. Benedict and Cathcart: Carnegie Institution of Washington, Pub. No. 187.

35. Henderson and Prince: *Am. Jour. Physiol.*, 1914, xxv, 106. The work of Murlin and Greer is incorrectly quoted in this paper.

36. Markwalder and Starling: *Jour. Physiol.*, 1914, viii, 348.

Murlin³⁷ and by Bailey and Murlin¹ of expressing the metabolism determined in hourly periods on the basis of an hour, whether dealing with a unit of weight or a unit of surface, is preferable.

From the last two columns in Table 5 may be seen what percentage of the total potential energy of the food in twenty-four hours would be utilized *in combustion* if the condition shown to the left of the table were to continue throughout. It may be of some interest practically to know that a child of, say, 2 months, fed 409 calories in twenty-four hours, utilized 74 per cent. of this energy (E. H.) for combustion alone even while sleeping, or that a child (J. S.) of 1 year (underweight) fed 462 gross calories is not getting food enough, if he is "restless and fretful more than two-thirds of the time," to support combustion alone.

METABOLISM IN RELATION TO SURFACE AREA

In order to have a satisfactory basis for comparison of the metabolism of the different children only the best sleeping periods (Table 6) have been selected, that is, those periods when sleep was either continuous throughout or was interrupted for only a few minutes. In one instance (C. M., March 26) the child, though awake for fifteen minutes of the period included, was lying very still, feeling drowsy and in reality in the process of falling asleep. The graphic records in these experiments made it possible to mark the very moment when a child fell asleep, or awoke.

The different formulas employed in the calculation of the surface area of children and their origin are too well known to require discussion at this time. Benedict and Talbot¹⁹ have covered the ground historically very recently. What remains is to discover *first* whether any such formula has any value in relation to the metabolism of children, and *second*, if so, which formula is best. It is not necessary to enter into a discussion as to whether one formula or the other best represents the actual surface area. That can be settled only by more actual measurements. Howland and Dana³⁸ have shown the range of variation of the fourteen actual measurements now on record. Applying these formulas and finding the average deviation from the mean of the actual metabolism in each instance, should enable us to judge which formula is of the greatest value as a criterion, whether it expresses the actual surface area or not. It is possible that the metabolism of the child exposed to a temperature of 27 to 29 C., at which chemical regulation does not enter (Rubner), is not at all proportional to the surface area, although there can be no doubt that

37. Carpenter and Murlin: Arch. Int. Med., 1911, vii, 184.

38. Howland and Dana: AM. JOUR. DIS. CHILD., 1913, vi, 33.

TABLE 6. METABOLISM IN RELATION TO SURFACE AREA, ARRANGED ACCORDING TO AGE *

| Name and Age | | | Condition | Date | Period | Weight, Gm. | Surface Area in Square Meters | | | Cal. per Hour | Calories per Square Meter and Hour | | Calories per Square Meter and 24 Hours | |
|-------------------|---|------|-----------|-------|--------|----------------|-------------------------------|---------------------------------|--------------------------------------|------------------|---------------------------------------|----------|---|-------|
| | | | | | | | $11.0 \sqrt{W}^2$ (Meeh) | $10.3 \sqrt{W}^2$ (Lissauer) | $10.3 \sqrt{W}^2$ (Meeh and Dana) | | Meeh | Lissauer | Howland and Dana | |
| 1914 | | | | | | | | | | | | | | |
| A. S., 2 mos. | Normal, over- weight | 2/11 | I | 5,810 | 0.384 | 0.333 | 0.354 | 12.00 | 31.2 | 26.05 | 33.90 | 749 | 861 | 811 |
| | | 2/16 | I | 5,692 | 0.379 | 0.328 | 0.348 | 11.78 | 31.05 | 25.89 | 33.85 | 715 | 801 | 812 |
| W. L., 2 mos. | Normal, near av. weight | 3/24 | I | 4,364 | 0.313 | 0.271 | 0.283 | 16.59 | 33.74 | 38.98 | 37.31 | 810 | 936 | 895 |
| | | 3/25 | I | 4,371 | 0.318 | 0.275 | 0.284 | 10.71 | 33.76 | 39.01 | 37.82 | 810 | 936 | 907 |
| E. H., 2½ mos. | Normal, aver- age weight | 3/26 | I | 4,350 | 0.317 | 0.271 | 0.283 | 10.75 | 33.90 | 39.14 | 37.99 | 813 | 939 | 912 |
| | | 6/24 | I | 4,690 | 0.339 | 0.287 | 0.299 | 12.68 | 38.03 | 43.94 | 42.41 | 942 | 1,055 | 1,018 |
| E. N., 3 mos. | Normal, un- derweight | 6/26 | II | 4,657 | 0.332 | 0.287 | 0.299 | 12.90 | 38.96 | 43.92 | 43.45 | 935 | 1,080 | 1,043 |
| | | 3/18 | I | 4,115 | 0.305 | 0.264 | 0.273 | 10.53 | 35.38 | 40.87 | 39.74 | 849 | 981 | 953 |
| C. P., 3 mos. | Marasmus | 3/19 | I | 4,117 | 0.307 | 0.266 | 0.273 | 10.47 | 34.88 | 40.30 | 39.25 | 837 | 967 | 942 |
| | | 2/27 | I and II | 2,492 | 0.217 | 0.188 | 0.192 | 7.25 | 33.42 | 38.61 | 37.76 | 802 | 926 | 906 |
| C. D., 4 mos. | Normal, un- derweight | 3/3 | I and II | 2,515 | 0.220 | 0.190 | 0.195 | 7.39 | 33.58 | 38.80 | 37.90 | 805 | 931 | 909 |
| | | 6/11 | I | 3,375 | 0.298 | 0.231 | 0.256 | 9.265 | 34.58 | 39.96 | 39.24 | 830 | 959 | 942 |
| M. M., 5¼ mos. | Overweight; positive von Pirquet; no fever | 6/18 | II | 3,440 | 0.271 | 0.231 | 0.233 | 10.79 | 39.79 | 45.97 | 45.15 | 955 | 1,103 | 1,084 |
| | | | | | | | | 10.67 | 38.45 | 45.46 | 44.64 | 923 | 1,091 | 1,072 |
| C. M., 10½ mos. | Normal, over- weight | 6/29 | I | 6,470 | 0.413 | 0.358 | 0.385 | 16.32 | 39.46 | 45.59 | 42.39 | 947 | 1,095 | 1,016 |
| | | 6/30 | II | 6,460 | 0.412 | 0.357 | 0.385 | 16.92 | 40.91 | 49.27 | 43.92 | 981 | 1,135 | 1,053 |
| W. S., 11-12 mos. | Normal, av. weight | 3/25 | I and II | 9,382 | 0.729 | 0.458 | 0.526 | 24.35 | 46.00 | 53.18 | 46.39 | 1,104 | 1,277 | 1,110 |
| | | 3/26 | III | 9,465 | 0.732 | 0.461 | 0.530 | 24.69 | 45.24 | 52.37 | 45.45 | 1,086 | 1,255 | 1,091 |
| J. S., 12 mos. | Normal (?), very much underweight | 2/10 | I | 9,373 | 0.729 | 0.457 | 0.526 | 23.88 | 45.14 | 52.15 | 45.40 | 1,083 | 1,251 | 1,090 |
| | | 2/11 | I | 9,440 | 0.731 | 0.460 | 0.529 | 23.51 | 44.23 | 51.10 | 44.41 | 1,062 | 1,227 | 1,067 |
| Mean | Mean, omitting J. S. | 2/28 | I | 9,555 | 0.536 | 0.464 | 0.534 | 26.72 | 49.87 | 57.59 | 50.03 | 1,197 | 1,382 | 1,291 |
| | | 3/21 | II | 5,892 | 0.384 | 0.333 | 0.353 | 20.59 | 53.59 | 61.91 | 58.32 | 1,286 | 1,486 | 1,400 |
| Algebraic mean | Average deviation from mean, omitting J. S. | 3/23 | I | 5,713 | 0.380 | 0.329 | 0.349 | 19.78 | 52.02 | 60.10 | 56.68 | 1,249 | 1,442 | 1,360 |
| | | | | | | | | 38.84 | 44.85 | 42.90 | | | | |
| | | | | | | | | | | | 37.96 | 43.90 | 38.82 | |
| | | | | | | | | | | | +4.96 | +3.52 | 0.07 | |
| | | | | | | | | | | | 10.03% | 11.37% | 0.07% | |
| | | | | | | | | | | | -0.659 | -0.58 | +2.43 | |

* Only best sleeping periods are included.

the metabolism of the child as compared with the adult is much more nearly proportional to Meeh's formula than to the body weight.³⁷

The abnormally high metabolism of Child J. S. (Case 5) seems to justify his exclusion from this comparison on the suspicion that

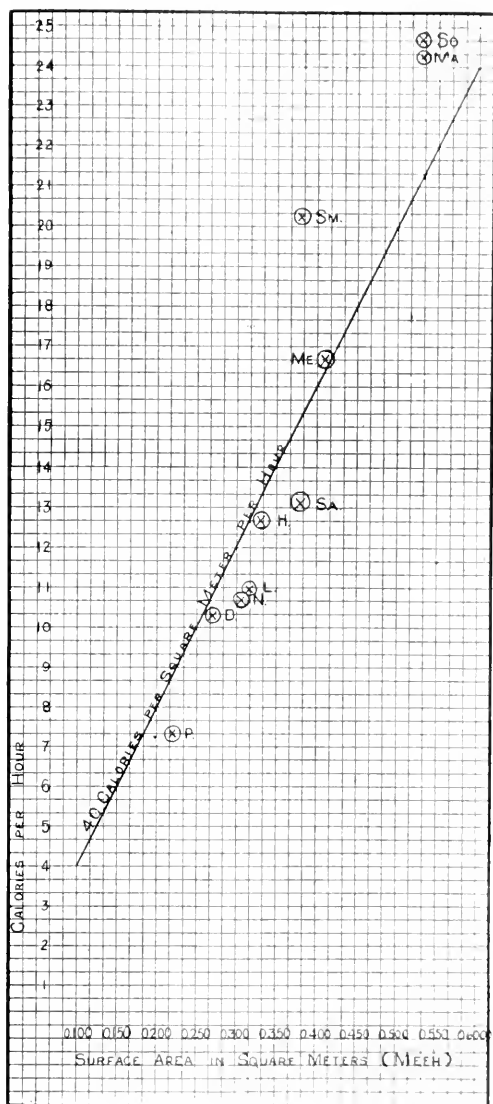


Fig. 7.—Showing relation of heat production to skin surface according to Meeh's formula. Authors' ten cases.

his trouble may have been due to hyperthyroidism. The mean metabolism of the nine remaining children based on the actual hourly determinations while the children slept, soon after feeding, and cal-

culated to the square meter basis is as follows: 37.96 calories for Meeh's formula; 43.90 calories for Lissauer's and 38.82 calories for Howland and Dana's equation. The mean deviation from this mean for the thirty-two hourly periods is ± 3.81 Cal., or 10.03 per cent. for Meeh's formula; ± 4.96 Cal., or 11.3 per cent. for Lissauer's and ± 3.52 Cal., or 9.04 per cent. for Howland and Dana's. For all of these formulas, therefore, the mean deviation from the mean is in the neighborhood of 10 per cent. The extreme deviations, however, are much greater (Table 6) namely: -6.91 to $+11.41$ calories per square meter, or -18.2 per cent. to $+31.4$ per cent. for Meeh's; -8.02 to $+13.6$ calories or -18.3 per cent. to $+31.2$ per cent. for Lissauer's; and -4.97 to $+11.21$ calories or -12.8 per cent. to $+28.9$ per cent. for Howland and Dana's. On both counts the equation of Howland and Dana lies a little nearer the actual facts of metabolism than the others.

The algebraic mean, however, for the present series of observations throws the favor to Meeh's formula. This lies at $-.059$ calories or very near the zero point; for Lissauer's it lies at -0.58 calories and for Howland and Dana's at $+2.43$ calories. It is a curious coincidence that an equation so constructed as to give a "gross error" (algebraic deviation from the mean) of zero, as an expression of the actual surface areas as found, should give, when used as a unit for the actual metabolism, the largest algebraic deviation. This but emphasizes the inference that the metabolism for this series of children, at least, is not very closely parallel to the surface area as found by the existing measurements. Nothing more should be deduced from the data here presented. The entire discrepancy may possibly be explained by the fact that the majority of the actual measurements were made on atrophic or underweight children,³⁹ while only three out of the nine children here averaged were underweight.

The conclusion of the inquiry in connection with the surface area, so far as these observations go, is (1) that the mean deviation from the arithmetical mean (probably the best criterion of the worth of a formula) is least with the equation of Howland and Dana, but (2) that with Meeh's formula the algebraic mean lies nearest the zero point.

A graphic representation of the metabolism in relation to surface area according to Meeh's formula is shown in Figure 7. The distribution would be essentially the same for either of the other formulas. The position of each child on the chart represents calories per square meter per hour. The diagonal line represents approximately the mean for the ten children. It is evident at a glance that the older children have the higher metabolism per unit of surface. The only cases which

39. Benedict and Talbot: Carnegie Pub. No. 201, table, p. 164.

do not exceed the resting metabolism of a healthy adult are the atrophic child C. P., 3 months, and the normal boy W. L., 3 months; C. D. (underweight) at 4 months of age has a metabolism of 37.60 calories; M. M., at nearly 6 months, a metabolism of 40; the girl C. M. at 10½ months a metabolism of 45.7 and W. S. at 12 months a metabolism of 46.4 calories per square meter and hour. This is brought out clearly in Table 7, arranged according to age.

TABLE 7.—SUMMARY OF SLEEPING PERIODS, SHOWING RELATION OF HEAT PRODUCTION TO BODY WEIGHT AND SURFACE AREA (MECH)

| Name | Nutritive Condition | Age, Months | Average Net Weight, Gm. | Cal. Per Hour | No. of Periods Averaged | Calories Per Kg. and Hour | Cal. Per Sq. Meter (Meeh) and Hour |
|--------------------------|--|-------------|-------------------------|---------------|-------------------------|---------------------------|------------------------------------|
| A. Sa. | Normal; overweight | 2 | 5,730 | 13.16 | 4 | 2.30 | 34.73 |
| W. L. | Normal; slightly below aver. weight | 2 | 4,362 | 10.68 | 3 | 2.45 | 33.80 |
| E. H. | Normal; av. weight | 2½ | 4,673 | 12.58 | 4 | 2.71 | 37.84 |
| E. N. | Normal; underweight | 3 | 4,132 | 10.65 | 4 | 2.59 | 34.99 |
| C. P. | Atrophic | 3 | 2,488 | 7.32 | 4 | 2.94 | 33.50 |
| C. D. | Normal; underweight | 4 | 3,410 | 10.24 | 3 | 3.00 | 37.60 |
| M. Me. | Normal; (?) positive v. Pirquet; av. wt. | 5¾ | 6,456 | 16.62 | 4 | 2.56 | 40.21 |
| C. Ma. | Normal; overweight | 10½ | 9,424 | 24.26 | 3 | 2.49 | 45.74 |
| W. So. | Normal; av. weight | 11½-12 | 9,456 | 24.70 | 3 | 2.51 | 46.41 |
| J. Sm. | Normal (?); very much underweight | 12 | 5,757 | 20.16 | 2 | 3.51 | 52.89 |
| Mean of all cases..... | | | | | | 2.75 | 39.76 |
| Mean omitting J. S. | | | | | | 2.63 | 38.31 |
| Mean deviation | | | | | | 0.163 | 3.87 |
| | | | | | | (6.2%) | (10.1%) |

Any difference in the dynamic action of the food (richer in carbohydrates) given to the younger children as compared with that (richer in protein and fat) given to the older children would favor the younger, that is, the dynamic action of the carbohydrate (probably) would be greater. On the other hand, the older children, C. M. and W. S., were a little more restless than the younger (Table 5). These two sources of possible discrepancy would tend to neutralize each other, and it is therefore clear that the recently fed, healthy, growing child at 1 year of age has, while asleep, a heat production considerably higher per unit of surface than that of a child up to 6 months, or than that of the adult; while the child from 2 to 4 months of age has a metabolism per unit of surface about the same as that of the adult⁴⁰ (1) (34 calories per square meter per hour).

40. Cf. Carpenter and Murlin: Note 37. McCrudden and Lusk: Jour. Biol. Chem., 1913, xiii, 447. Du Bois, Eugene F.: The Total Energy Requirement in Disease as Determined by Calorimetric Observations, Jour. Am. Med. Assn., Sept. 5, 1914, p. 827.

Benedict and Talbot⁴¹ express the opinion that age is not a determining factor and yet they present a table of six normal infants in which there is a clear difference between infants under 6 months and those over 6 months. In another table (page 167) they compare the metabolism of infants of different ages but of the same weight and height, showing that in every instance the older child has the higher metabolism. Their explanation is that the older infant has a deficiency of fat and therefore a greater proportion of active protoplasmic tissue. We have seen, however, that fat does not replace active protoplasm (the nitrogen content of the body must be taken as a measure of the mass of protoplasm), but replaces water. Benedict and Talbot's table could therefore be used equally well to prove that the older infant, within the range from 2 months to 12 months, has a specifically higher coefficient of metabolism, or else has the same coefficient and the heat production is greater because the heat loss is greater.

We have calculated the heat production of all of Benedict and Talbot's normal infants of average weight, or nearly so, as given in their longer table⁴² to the basis of a square meter and hour and have

TABLE 8.—CALORIES PER SQUARE METER PER HOUR

| 2 Months | | 3 Months | | 4 Months | | 6 Months | | 7 Months | | 9 Months | | 10-11 Months | | 12 Months | |
|----------|------|----------|------|----------|------|----------|------|----------|------|----------|------|--------------|------|-----------|------|
| B. D. | 33.3 | E. F. | 29.5 | L. R. B. | 35.2 | M. M. | 40.2 | P. W. | 41.6 | R. L. | 41.3 | E. A. | 37.8 | W. S. | 46.4 |
| F. D. | 37.3 | A. S. | 32.2 | M. C. | 35.3 | | | | | R. S. | 40.2 | C. M. | 45.7 | | |
| L. L. | 31.7 | E. R. | 36.4 | R. E. | 38.3 | | | | | | | | | | |
| W. L.* | 33.8 | E. N. | 34.9 | D. O. | 35.2 | | | | | | | | | | |
| E. D. | 37.8 | | | | | | | | | | | | | | |
| A. S. | 34.7 | | | | | | | | | | | | | | |

* Benedict and Talbot's cases light face. Authors' cases full-faced type.

compared them with the normals of the present series with the result shown in Table 8.

The average of the fourteen cases up to and including 4 months of age is 35.4 calories per square meter and hour; the average of the seven cases from 6 months to 12 months inclusive is 41.9 calories per square meter and hour. The mean deviation in the first group is 5.4 per cent.; in the second group 5.7 per cent. There is some indication that the increase is a progressive one with increasing age; but the decision of this important matter must wait on further observations.

41. Benedict and Talbot: Carnegie Institution of Washington, Pub. No. 201, p. 165.

42. Benedict and Talbot: AM. JOUR. DIS. CHILD., 1914, viii, 1.

METABOLISM IN RELATION TO BODY WEIGHT

Figure 8 represents on the same scale as Figure 7 the heat production per kilogram and hour. The diagonal in this case (2.5 calories per kilogram and hour) is not quite the mean of all cases (Table 7), but is chosen as a convenient reference line. That the heat production in this series of ten children between the ages of 2 months and 12 months and varying in nutritive condition from extreme atrophy to extreme fatness, is more nearly proportional to weight than to surface area is seen from Table 7. Omitting J. S., the mean deviation from the mean (2.63 calories per hour), on the basis of weight is 6.2 per cent.; while on the basis of surface it is 10.4 per cent.

One must be on guard here against the hasty conclusion that metabolism in general is more nearly proportional to weight than to surface area. Taking the entire group of nine children this is unquestionably true "on the face of the returns." It would not be true, however, as regards any group of the same age. It has been seen that the average heat production of children above 6 months of age is higher, on the basis of a unit of surface, than is that of children ranging from 2 to 4 months, inclusive. It will be interesting now to make the same comparison on the basis of weight (Table 9).

TABLE 9.—CALORIES PER KILOGRAM AND HOUR

| 2 Months | | 3 Months | | 4 Months | | 6 Months | | 7 Months | | 9 Months | | 10-11 Months | | 12 Months | |
|----------|------|----------|------|----------|------|----------|------|----------|------|----------|------|--------------|------|-----------|------|
| B. D. | 2.33 | E. F. | 1.84 | L. R. B. | 2.30 | M. M. | 2.56 | P. W. | 2.57 | R. L. | 2.50 | E. L. | 2.13 | W. S. | 2.61 |
| E. D. | 2.63 | A. S. | 2.11 | M. C. | 2.23 | | | | | R. S. | 2.22 | C. M. | 2.56 | | |
| L. L. | 2.18 | E. R. | 2.63 | R. E. | 2.67 | | | | | | | | | | |
| W. L.* | 2.45 | E. N. | 2.59 | D. O. | 2.40 | | | | | | | | | | |
| E. H. | 2.71 | | | | | | | | | | | | | | |
| A. S. | 2.30 | | | | | | | | | | | | | | |

* Benedict and Talbot's cases light-faced type. Authors' cases full-faced type.

The average for the group of fourteen younger infants is 2.38 calories per kilogram and hour, with a mean deviation from this of 0.19 calorie or 8 per cent. The average for the group of older infants is 2.45 calories with a mean deviation of 0.159 calorie, or 6.5 per cent. The percentage deviation being greater in both groups on the basis of weight than on the basis of surface, it follows that the metabolism in both is more nearly proportional to surface. Incidentally also it is clear that even on the basis of weight the metabolism of the older infants is somewhat greater than that of the younger.

SUMMARY OF ALL REPORTED CASES

Figure 9 exhibits the variations in the heat production per unit of weight of all the children whose metabolism has been determined by the indirect method of Voit and Pettenkofer or according to the prin-

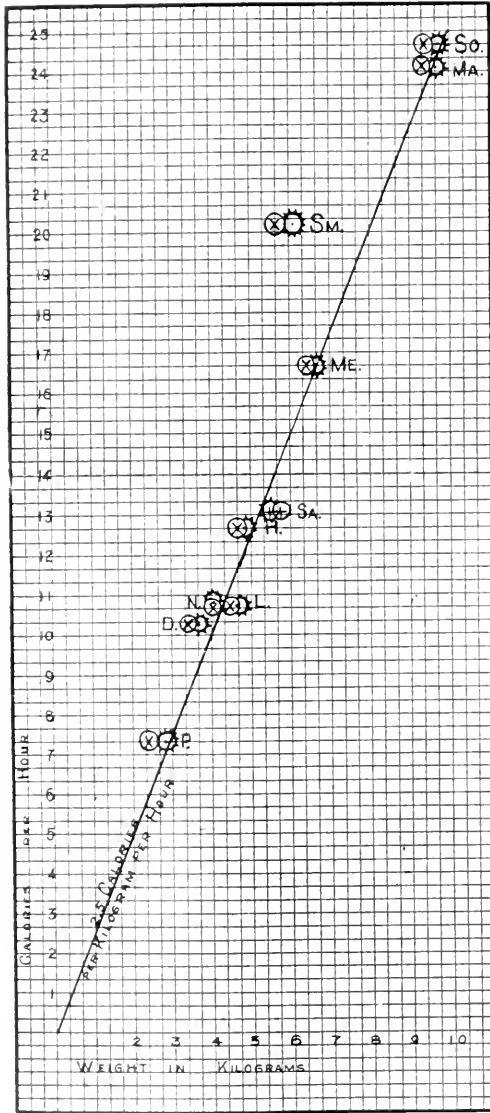


Fig. 8.—Showing relations of heat production to bodyweight, and effect of using "approximate specific gravity." Authors' ten cases. The plain circles represent the number of calories per kilogram and hour; the starred circles represent the same after first correcting the weight by multiplying by the approximate specific gravity. See, however, Note 12.

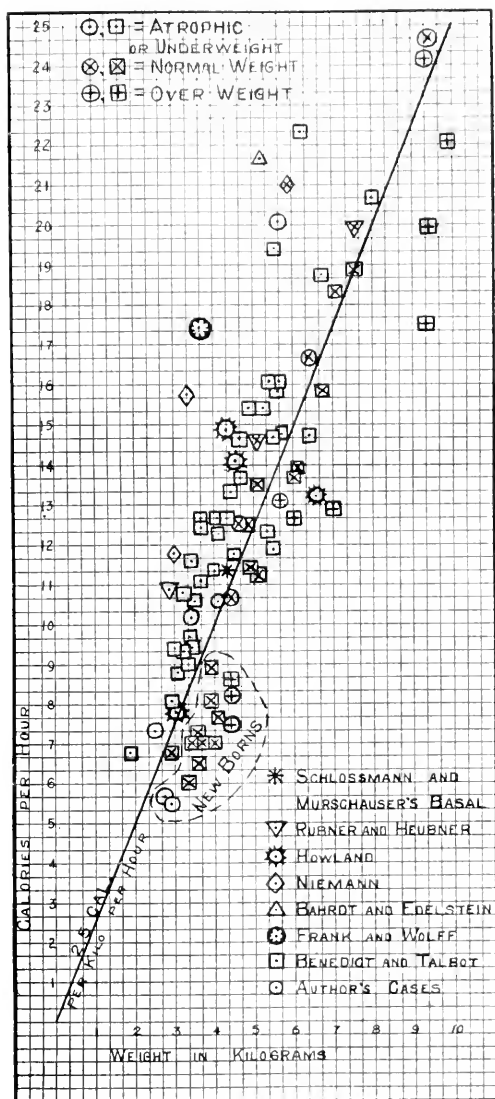


Fig. 9.—Showing relation of heat production to body weight. All infants whose metabolism has been studied by von Pettenkofer or Regnault-Reisch methods.

ciple of Regnault and Reiset. Figure 10 exhibits the heat production for the same cases on the basis of a unit of surface according to Meeh's formula. In both charts the atrophic or underweight infants are designated by a dot; thus, \odot or $\boxed{\bullet}$; those of normal weight by a cross \otimes , \boxtimes , etc., and the overweight infants by a cross thus, \bigcirc , \square , etc. In Figure 9 it may be seen that with but three exceptions (all in Benedict and Talbot's series) the heat production of the atrophic or underweight infants is above 2.5 calories per kilogram per hour; the normals lie close to this line and the overweights with a single exception (C. M. of our series) lie below the line. Properly speaking, only the infants whose heat production has been measured while sleeping (those of Howland, Benedict and Talbot and ours) are comparable. The mean for all the infants between the ages of 2 months and 1 year comprised in this way (sixty-one in all) is 2.7 calories per kilogram an hour. The average deviation from this mean among the sixty-one infants is 0.326 calories, or 12.1 per cent. The mean for the same list of infants on the basis of a square meter of surface (Meeh) is 39.3 calories per hour; while the average deviation from this mean is 4.34 calories or 11 per cent. Taking all the American infants within the range of from 2 to 12 months studied while sleeping, therefore, the heat production is slightly more uniform on the basis of Meeh's formula than on the basis of weight.

DISCUSSION

Judging by the comparison contained in these charts as well as by the summary of Bahrdrf and Edelstein⁴⁰ there is a considerable discrepancy in the application of the law of surface area to children of different age and different nutritive condition. Benedict and Talbot⁴² having before them all of the data, save those from the ten cases of the present series, reached the rather sweeping conclusion that there is no correlation between the heat production and the surface area. Such a conclusion is not, however, justified by the facts; for an average variability of ± 10 per cent. is not so excessive as biological laws go.⁴³

43. One reason why the charts of Benedict and Talbot seem to show "absolutely no correlation" either between body weight and heat production or skin surface and heat production is the fact that the zero point for only one variable is shown. Another reason is the duplication of ordinates. For example, when one compares the body weight as ordinates with the calories per kilogram and twenty-four hours as abscissae, there is a duplication of weight in both variables. The better way to plot such results is to choose two supposedly independent variables as ordinates and abscissae having a common zero point. Still further, if Benedict and Talbot had distinguished in their chart the atrophic or underweight children from the normal and overweight cases, they would have discovered the interesting facts mentioned under "Summary of All Reported Cases."

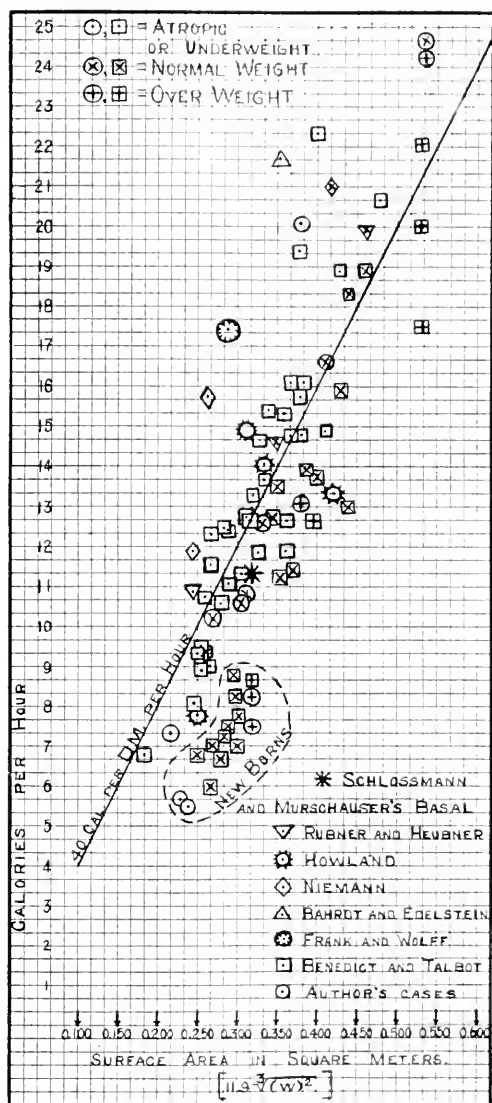


Fig. 10.—Showing relation of heat production to skin surface. All infants whose metabolism has been studied by von Pettenkofer or Regnault-Reisch methods.

Curiously enough, these authors appear to regard their findings on infants as a crucial test of the law of surface area; whereas the conditions necessary for its proof, recognized by Rubner⁴⁴ from the first, have not been (and could not be with the material selected) complied with. Rubner has always recognized the fact that the proof of the law of surface area requires similar physiologic conditions. Speaking of its applicability to children in 1906, he⁴⁵ says:

"Das Oberflächengesetz gilt unter allen physiologischen Lebensbedingungen: In seinem Beweise ist aber sinngemässe Voraussetzung, dass nur Organismen mit gleichartigen physiologischen Leistungen, was Ernährung, klimatische Einflüsse, Temperament und Arbeitsleistung betrifft, verglichen werden."

Rubner has never yet admitted that age is a variable factor in its influence on metabolism. But from the results presented by Benedict and Talbot and by Bailey and Murlin¹ on new-born infants, the differences cited in Table 7 and those recorded by Rubner himself, by Sondén and Tigerstedt, Magnus-Levy and Falk and McCrudden and Lusk, it is impossible not to see a functional variation with age.

The general law of surface area as applied to animals of the same species but different weight rests on a very secure observational foundation.⁴⁶ Whether it can be said also to apply uniformly to the entire class of mammals is doubtful.⁴⁷ Specific differences in the influence of certain organs such as the thyroid, differences in coat covering, proportion of parts, rate of growth, etc., probably must be reckoned with. What remains to be discovered in the application of the law to the human species is the cause of the discrepancies, and it is to this question that the present inquiry has been directed.

The specific question which we have been concerned with is the influence of body fat. The presence of fat always reduces the metabolism per unit of weight and, according to Meeh's formula, it frequently reduces the metabolism per unit of surface; while its absence produces the opposite effects. At the beginning of this investigation we supposed that fat in general is merely added to the protein, that is, active protoplasm, and it was for this reason that an effort was made to employ the specific gravity as a measure of the proportion

44. Rubner: *Ztschr. f. Biol.*, 1885, xxi, 337.

45. Rubner: *Arch. f. Hyg.*, 1906, lxvi, 89.

46. Cf. e. g. Rubner: *Ztschr. f. Biol.*, 1885, xxi, 337, Sondén and Tigerstedt: *Skand. Arch. f. Physiol.*, 1895, vi, 1. Magnus-Levy and Falk: *Arch. f. Anat. u. Physiol.*, 1899, *Phys. Abt. Suppl.*, p. 314. Slowtsoff: *Pfluger's Arch. f. d. ges. Physiol.*, 1903, xcv, 158. Kettner: *Arch. f. Anat. u. Physiol.*, *Phys. Abt.*, 1909, p. 447. Carpenter and Murlin: *Arch. Int. Med.*, 1911, vii, 184. Hill and Hill: *Jour. Physiol.*, 1913, xlv, 81. Du Bois: *Jour. Am. Med. Assn.*, Sept. 5, 1914, p. 827.

47. Pütter: *Ztschr. f. allg. Physiol.*, 1911, xii, 125.

between the two. Before the work was completed, however, it became clear from the analyses of infants of widely different nutritive condition, reported by Ohlmüller, Sommerfeld, Steinitz, and Steinitz and Weigert that fat replaces water; hence, the specific gravity, even could it be determined accurately, could not give a measure of the proportion between active and inactive tissue. This test, therefore, fails completely; for although the volume of the body as found by Kastner's method does appear to have an inverse relation to the heat production, it probably is not because of the proportion of fat present (see Figure 9).

Evidence has been presented that the metabolism increases from birth up at least to 1 year of age. The difference in nitrogen content between the new-born and infants from 2 to 4 months of age (Table 1) is due in part to loss of water; hence it seems possible that the coincident increase in metabolism may be explained by a loss of water and gain in the activity of the protoplasm. But the constancy of the protein content between children of the same age (nearly) but of different nutritive condition seems to make it clear that the proportion of active protoplasm as compared with fat cannot be the cause of the observed discrepancies between thin and fat children. What better criterion of protoplasmic mass could be had than protein content of the body? If this point is well taken, then the presence of fat must operate in one of two ways: either it affects the heat production by reducing the quality of the active protoplasm, or it affects merely the heat loss.

SUMMARY

1. Ten infants ranging in age from 2 months to 12 months and in nutritive condition from the last stage of marasmus to considerably overweight, have been compared as to their heat production both on the basis of weight and of surface area.

2. The heat production was calculated from the oxygen absorption with knowledge of the respiratory quotient (corrections being made for temperature, barometric pressure, and composition of the air) and from the nitrogen of the urine.

3. Graphic records of the respiration (in all cases) and of the pulse (in all but three cases) were obtained, these recording devices serving also to exhibit plainly on a smoked paper the degree of quiescence of the subject.

4. The approximate specific gravity was determined by Kastner's method in the hope that it might serve as a measure of the proportion of fat to active tissue.

5. The child was fed immediately before the observation each day and in nearly every experiment slept at least one, often two hours, while the respiratory exchange was being measured.

CONCLUSIONS

1. The specific gravity, even if accurately measured, cannot serve as a measure of the proportion of fat to active tissue, because, according to the analyses of Sommerfeld, Steinitz, and Steinitz and Weigert the fat replaces only water, the nitrogen remaining constant for children of widely different nutritive condition and nearly the same age.

2. The heat production for the sleeping period averages for the ten children 2.7 calories per kilogram and hour. It is highest on this basis for the atrophic and underweight children and lowest for the fattest child.

3. On the basis of a square meter of surface the heat production of normal children shows a decided increase from the early months (2-4) to the later months (6-12) of the first year. The average of all the ten children is 39.7 calories.

4. The average deviation from the mean heat production in all sleeping periods is about ± 10 per cent. for each of the several formulas expressing the relation of surface area to weight (Meeh, Lissauer, Howland and Dana). The algebraic mean deviation is least with the formula of Meeh.

5. Almost identically the same average heat production per unit of weight and per unit of surface is obtained when all the infants between 2 months and 12 months in Howland's, Benedict and Talbot's and our series (sixty-one in all) are compared, i. e., 2.7 calories per kilo and hour, 39.3 calories per square meter and hour (Meeh). On the unit of weight all but three of the atrophic and underweight children (forty-eight in all) lie above the line represented by 2.5 calories per kilogram and hour; all the normals (eighteen) lie near this line; and all but one of the overweight infants (five) lie below the line. Two and one-half calories per kilogram and hour or 60 calories per kilogram and twenty-four hours may therefore be called tentatively the "normal heat production" of recently fed, sleeping infants between 2 months and 1 year of age. Included in this figure is whatever dynamic action the foods themselves may have; otherwise the figure is minimal. Hard crying may increase the metabolism as much as 40 per cent.; the requirement for growth and an allowance for non-absorption must be added.

6. The average deviation from the mean on the basis of weight for all these children is 12.1 per cent.; on the basis of surface area (Meeh) 11 per cent. For smaller age groups of normal children the deviation is considerably less on the basis of surface area than on the basis of weight. Taking into account possible variations in the dynamic influence of food, these results must be regarded as confirmatory of the "law" of surface area of Rubner.

7. There seems to be no sufficient reason, however, for estimating the food requirements of infants on the basis of surface area rather than on the basis of weight.

WHEY IN INFANT-FEEDING

STUDIES OF INFANT-FEEDING: FIFTH PAPER *

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GENEVA, N. Y. BOSTON BOSTON

INTRODUCTION

The investigations of Osborne and Mendel¹ have shown the important part taken by the whey salts in the growth and development of the young rat, and Holt, Levene and others² have shown that a proper adjustment of the relation between the amount of whey and some of the other constituents present in infant-foods is quite necessary in order to prevent disturbances in the normal metabolism and physical condition of artificially fed infants. It has, therefore, become necessary, in our studies of infant-feeding, for us to know more about the significance of whey, especially in connection with the treatment of certain types of infectious diarrhea, fat intolerance and regulation of feeding, and the investigations reported here are some of the results obtained by us in this connection.

The baby used for this investigation was of a rather happy disposition and had been used by us, some months previous to the present observation, for other metabolism work. He had been discharged from the hospital after a period of feeding regulation, and was readmitted on July 9, 1913, suffering from intestinal indigestion due to over-feeding.

METABOLISM OBSERVATION

The investigation began with the admission of the baby to the hospital on July 9 and may be divided into six periods as indicated.

* Submitted for publication Dec. 14, 1914.

* The expense of this investigation was defrayed by the Boston Floating Hospital, Boston, Mass. The chemical work was done in the Biochemical Laboratory of the Harvard Medical School, Boston, Mass. We wish to thank Dr. Otto Felin for his courtesy in extending this privilege to us.

* Bowditch, H. I. and Bosworth, A. W.: Casein in Infant-Feeding: Experiments in Exact Percentages, *AM. JOUR. DIS. CHILD.*, December, 1913, p. 364; Rules for Calculating the Approximate Composition of Milk from the Specific Gravity and Percentage of Fat as Determined by the Babcock Method, *ibid.*, March, 1914, p. 244. Bosworth, A. W., and Van Slyke, L. L.: Why Sodium Citrate Prevents Curdling of Milk by Rennin, *ibid.*, April, 1914, p. 298. Bosworth, A. W., Bowditch, H. I., and Ragle, B. H.: Casein in Infant-Feeding: The Preparation of Dry Powdered Paracasein, *ibid.*, August, 1914, p. 120.

1. Publication No. 156 of the Carnegie Institute.

2. Holt, Levene et al.: *AM. JOUR. DIS. CHILD.*, 1912, iv, 265.

First Period, 6 p. m. July 9 to 6 p. m. July 12

From 6 p. m. July 9 until 10 a. m. July 11 (forty hours) the child received only sterile water. From 10 a. m. July 11 to 6 p. m. July 12 (thirty-two hours) the food consisted of a mixture of 840 c.c. of whey, 420 c.c. of breast-milk and 420 c.c. of water and was divided into ten feedings. The child was on the metabolism frame during all three days.

The high output of uric acid, creatinin and creatin during the fast indicates a high endogenous metabolism and is followed by a higher excretion of these substances on the administration of food; the excretion of nitrogen, however, is lowered during the first day following the fast, indicative of a replacement of the nitrogen lost during the endogenous metabolism of the fast. During the fast the chlorin excreted was very small in amount, and both indican and acetone were detected in the urine. The child also had an acetone breath.

Second Period, 6 p. m. July 12 to 6 p. m. July 22

A period during which the food was changed several times in order to find a mixture suitable for the child. The child was not on the metabolism frame and no analytical data were secured during this period.

Third Period, 6 p. m. July 22 to 6 p. m. July 26

The child had recovered from his intestinal trouble and was receiving the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

| | |
|-------------------------|----------|
| 10 per cent. cream..... | 160 c.c. |
| Buttermilk | 800 c.c. |
| Sterile water | 640 c.c. |
| Milk-sugar | 53 gm. |

Seven feedings of 210 c.c. each every twenty-four hours. Approximately 637 calories or 145 calories per kilo body weight.

As he seemed to be in good condition and gaining in weight on this food, he was placed on the metabolism frame at 6 p. m. July 22. During this period he continued to receive the food indicated above and the urine and feces were collected and examined in order to furnish data representing his normal nitrogen metabolism. During this period the body weight increased 165 gm., and average of 41.2 gm. per twenty-four hours. He was well in every respect.

Fourth Period, 6 p. m. July 26 to 6 p. m. July 29

The child was not on the frame during this period but received the same food given in the preceding period. No macroscopic or microscopic evidence of fat, carbohydrate or protein indigestion was found.

Fifth Period, 6 p. m. July 29 to 6 p. m. August 7

The child was again placed on the frame and the food received was made up according to the following formula: Fat, 1 per cent.; sugar, 6 per cent.; protein, 2 per cent.

| | |
|-----------------------------------|------------|
| 10 per cent. cream..... | 161 c.c. |
| Sterile water | 1,439 c.c. |
| Lactose | 89 gm. |
| Dry paracasein ³ | 25 gm. |

Seven feedings of 210 c.c. each per twenty-four hours.

This mixture contained about the same amounts of fat, sugar and protein as the mixture given in the two preceding periods. The amount of protein ingested in twenty-four hours was less than in the case of the food made with

3. A method of preparing dry powdered paracasein has been given in a previous paper, *AM. JOUR. DIS. CHILD.*, August, 1914, p. 120.

buttermilk. This was due to the fact that it was almost impossible to manipulate the feeding-bottles so that all the paracasein was removed with the liquid portion of the food.

The inorganic salts were very much decreased in this mixture. In the preceding periods the mixtures fed contained the salts carried in the 160 c.c. of cream and the 800 c.c. of buttermilk. In the present case all the inorganic salts were derived from the 161 c.c. of 10 per cent. cream. The response to this decrease in the inorganic salt intake is shown in the lower figures obtained during this period for sodium chlorid, phosphates and acidity. The food contained 0.116 gm. of sodium chlorid per twenty-four-hour quantity while the amounts excreted dropped from 0.326 gm. the first day to nothing on the eighth and ninth days, chlorin again appearing on the tenth day (the first day of the sixth period) even with a reduction in the chlorin intake on that day. This small chlorin excretion, zero for two days even, was not accompanied by any signs of physical discomfort.

During this period the body weight increased 120 gm., an average of 13.3 gm. per twenty-four hours.

Sixth Period, 6 p. m. August 7 to 6 p. m. August 14

From 6 p. m. August 7 and during this period the food given to the child was made according to the following formula: Fat, 2 per cent.; sugar, 6 per cent., protein, 2 per cent.

| | |
|-------------------------|------------|
| 32 per cent. cream..... | 54 c.c. |
| Sterile water | 1,546 c.c. |
| Lacto-c | 89 gm. |
| Dry paracasein | 28 gm. |

Seven feedings of 210 c.c. each per twenty-four hours.

This decreased the inorganic salts again and made the chlorin intake per twenty-four hours equal to 0.033 gm. of sodium chlorid, and the amounts excreted dropped from 0.148 gm. to 0 gm. on the fifth, sixth and seventh days. The child showed no particular discomfort as a result of this rather prolonged confinement on the metabolism frame, but on account of the loss of body weight it was thought best to discontinue the collection of urine and feces and remove the child from the frame at 6 p. m. August 14.

GENERAL DISCUSSION

In connection with the table which gives the result of our daily examination of the urines, we desire to call attention to the following points:

The acidity of the urines and the amounts of phosphates present decreased with the decrease in the amounts of whey ingested. This was to be expected as all the inorganic phosphates ingested were contained in the whey or cream used to make up the formulas. The amounts of organic phosphorus ingested were practically the same through all the periods.

The elimination of chlorin-free urine for two- and three-day periods without symptoms of any nature is worthy of note.

A very marked increase in the ammonia output during the sixth period of the experiment is noticeable. During the fifth period the whey in the 161 c.c. of 10 per cent. cream furnished considerable neutral salts of organic acids (citrates, albuminates, etc.), the bases of

TABLE 1.—SHOWING CHANGE IN COMPOSITION OF URINE AS A RESULT OF REDUCING THE INTAKE OF INORGANIC SALTS

| Date* | Body Weight, Gm. | Urine | | | | | | | | | | Average N, in Feeces, Gm. | |
|----------|------------------|--------------|------------------|------------------------|-------------------------------------|-----------------|--------------|----------------------------|----------------|----------------|----------------|---------------------------|--------------|
| | | Volume, C.c. | Specific Gravity | Total Acid, N/10, C.c. | P ₂ O ₅ , Gm. | Cl as NaCl, Gm. | Total N, Gm. | N as NH ₄ , Gm. | N as Urea, Gm. | Uric Acid, Gm. | Creatinin, Gm. | | Creatin, Gm. |
| | | | | | | | | | | | | | |
| 7/10† | 4,500 | 505 | 1.007 | 82.8 | 0.577 | 0.024 | 1.513 | 0.161 | 1.111 | 0.107 | 0.030 | 0.041 | |
| 7/11† | | 630 | 1.005 | 51.2 | 0.534 | 0.048 | 1.658 | 0.247 | 1.094 | 0.131 | 0.028 | 0.068 | |
| 7/12† | 4,540 | 670 | 1.005 | 141.7 | 0.574 | 0.206 | 1.294 | 0.110 | 0.884 | 0.243 | 0.037 | 0.065 | |
| 7/12-22† | | | | | | | | | | | | | |
| 7/23 | 4,480 | 700 | 1.006 | 127.4 | 0.810 | 0.913 | 1.372 | 0.319 | 0.806 | 0.065 | 0.029 | 0.026 | 0.365 |
| 7/24 | | 669 | 1.006 | 97.7 | 0.948 | 0.800 | 1.774 | 0.292 | 1.279 | 0.057 | 0.019 | 0.024 | 0.365 |
| 7/25 | | 980 | 1.006 | 156.8 | 1.129 | 1.180 | 2.387 | 0.274 | 1.949 | 0.084 | 0.021 | 0.030 | 0.365 |
| 7/26 | 4,615 | 900 | 1.007 | 134.6 | 1.161 | 1.509 | 2.550 | 0.300 | 2.051 | 0.084 | 0.021 | 0.034 | 0.365 |
| 7/26-29 | | | | | | | | | | | | | |
| 7/30 | 4,730 | 1,200 | 1.001 | 98.4 | 0.700 | 0.326 | 1.717 | 0.175 | | 0.052 | 0.022 | 0.020 | 0.173 |
| 7/31 | | 1,220 | 1.003 | 11.5 | 0.386 | 0.332 | 1.264 | 0.164 | 0.929 | 0.078 | 0.022 | 0.030 | 0.173 |
| 8/1 | | 1,300 | 1.002 | 41.6 | 0.328 | 0.110 | 1.092 | 0.175 | 0.815 | 0.053 | 0.023 | 0.020 | 0.173 |
| 8/2 | | 1,246 | 1.002 | 39.7 | 0.379 | 0.298 | 1.146 | 0.208 | 0.724 | 0.066 | 0.021 | 0.025 | 0.173 |
| 8/3 | | 1,076 | 1.003 | 12.8 | 0.317 | 0.223 | 1.079 | 0.216 | 0.713 | 0.057 | 0.019 | 0.022 | |
| 8/4 | | 670 | 1.003 | 21.1 | 0.233 | 0.115 | 0.925 | 0.173 | 0.522 | 0.015 | 0.018 | 0.021 | |
| 8/5 | | 1,170 | 1.003 | 56.2 | 0.370 | 0.017 | 1.409 | 0.216 | 0.963 | 0.081 | 0.029 | 0.028 | |
| 8/6 | | 1,060 | 1.003 | 33.9 | 0.357 | 0.000 | 1.076 | 0.261 | | 0.072 | 0.020 | 0.029 | |
| 8/7 | 4,850 | 1,000 | 1.003 | 33.9 | 0.357 | 0.000 | 1.076 | 0.261 | | 0.072 | 0.020 | 0.029 | |
| 8/8 | | 1,000 | 1.002 | 38.2 | 0.332 | 0.148 | 1.039 | 0.522 | 0.281 | 0.072 | 0.020 | 0.027 | |
| 8/9 | | 850 | 1.003 | 17.6 | 0.390 | 0.065 | 1.275 | 0.509 | | 0.081 | 0.020 | 0.015 | |
| 8/10 | | 970 | 1.003 | 26.6 | 0.317 | 0.007 | 1.249 | 0.194 | | 0.082 | 0.022 | 0.019 | |
| 8/11 | | 1,000 | 1.003 | 27.6 | 0.378 | 0.015 | 1.276 | 0.392 | 0.613 | 0.086 | 0.020 | 0.020 | |
| 8/12 | | 1,000 | 1.003 | 32.0 | 0.275 | 0.000 | 1.036 | 0.476 | | 0.087 | 0.017 | 0.015 | |
| 8/13 | | 900 | 1.005 | 28.8 | 0.203 | 0.000 | 1.411 | 0.731 | | 0.075 | 0.017 | 0.019 | |
| 8/14 | 1,510 | 760 | 1.003 | 33.4 | 0.357 | 0.000 | 1.105 | 0.655 | 0.378 | 0.092 | 0.020 | 0.017 | |

* Twenty-four hour period ending 6 p. m. † Traces of indican appeared in the urine on these days. ‡ Traces of acetone on these days.

which could be used to neutralize the acid bodies eliminated in the urine. During the sixth period, however, the intake of such base-carrying substances was much reduced, and sufficient bases were not ingested to neutralize the acid bodies eliminated in the urine. This resulted in an immediate increase in the amount of ammonia in the urine with a corresponding decrease in the urea. For the twenty-four hours ending at 6 p. m., August 7, the urine contained 0.261 gm. of nitrogen present as ammonia, and for the twenty-four-hour period ending at 6 p. m., August 8, the first day of the reduction of the intake of the salts to the lowest figure, the urine contained 0.522 gm. of nitrogen in the form of ammonia, an increase of 100 per cent. in one day.

It will be noticed that only a small part of the ammonia is necessary to neutralize the phosphates. Just what the nature of the acid bodies is we are not able to state. We did not detect the presence of acetone bodies in the urine at any time during this period.

The amounts of creatinin and creatin excreted during the fasting period were much above the normal as would be expected. During the other three periods the creatinin figures are strikingly uniform.

During the third period, when the food contained an excess of all constituents, the child increased in body weight an average of 41.2 gm. per twenty-four hours and the creatin output averaged 0.028 gm. per day. In the fifth period when the whey had been reduced to the amount carried in 161 c.c. of 10 per cent. cream, the average daily increase in body weight was reduced to 13.3 gm. and the average daily creatin excretion was 0.025 gm. In the sixth period there was an average daily decrease in body weight of 48.6 gm., and the average daily excretion of creatin was 0.019 gm. with a daily fluctuation giving figures between 0.027 and 0.015 gm.

The child received an abundance of fat, sugar and protein during all of the experiment; the whey constituents being under observation were of course the only variable. The observation seems to indicate, therefore, that the amount of whey received during the fifth period was not sufficient to promote the maximum growth, yet large enough to prevent an actual cessation of growth, while during the sixth period the amount of whey received was so small that growth was stopped and the body lost in weight. It might be claimed that the long confinement on the metabolism frame was responsible for the loss in weight during the last period, but in answer to this we can say that the baby was of exceptionally happy disposition, showed no signs of discomfort during all the investigation and was very carefully watched and cared for. We carried the observation as far as was advisable with a human subject, and feel that we have confirmed in this case the work of Osborne and Mendel in which they demonstrated the

necessity of whey salts to promote growth of the young when fed on pure materials — fats, carbohydrates and protein.

The investigation would also seem to bear out the theory that creatin excretion is in some way involved in growth and also to offer an explanation of the fact observed by others that the creatin excretion of growing infants varies from day to day. An infant normally grows quite rapidly, increasing several grams per day in body weight. If the food taken and retained during any day or series of days is not sufficient to meet all the demands of maximum growth, growth will fluctuate and a corresponding fluctuation in the creatin elimination will result.

This paper constitutes a report of a part of a series of investigations which is being conducted in connection with the regular clinical work of the Boston Floating Hospital.

TREPOXEMA PALLIDUM FOUND AT AUTOPSY, IN THE BLOOD-STREAM AND ELSEWHERE, IN A CASE OF CONGENITAL SYPHILIS

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It has been the experience that clinical histories, pathologic findings and the Wassermann test may indicate syphilis in many cases in which it is impossible to demonstrate the presence of *T. pallidum* in any of the tissues outside of the primary and secondary lesions accessible to external examination. This may in part be accounted for by the stage of the disease, the effects of treatment, and the difficulty encountered in getting the organisms present in a given preparation to reveal their presence when staining methods or silver impregnation are applied.

This disease, in both its acquired and its congenital forms, is perhaps as common on the Isthmus of Panama as elsewhere, yet it almost never happens that the demonstration of *T. pallidum*, either in smears or in sections, can be made from selected material taken at autopsy from the various tissues, such as liver, placenta, bone-marrow, spleen, heart, aorta, etc.

It is generally known that material from cases of congenital syphilis offers the best opportunities for such a demonstration; but how does the frequency of such findings compare with the incidence of this type of the disease or the frequency of positive responses to the Wassermann test?

We note that the *Journal of Pathology and Bacteriology*¹ publishes a list of rare materials wanted, and a request was made not long ago by a large institution for "congenital syphilitic liver, with spirochetes."

The results obtained in the case about to be described are so foreign to the usual results at Ancon in this respect that it is deemed worthy of some attention.

CASE REPORT

History No. 154570. The patient, a female child, 2 months old, of Panamanian parentage, was admitted to Ancon Hospital, Dec. 20, 1913. The father is a Spanish-Indian mixture, 32 years old, and is employed as a waiter. He had a chancre in June, 1910. Three months later a periostitis of the right tibia

1. Jour. Path. and Bacteriol., October, 1911.

was noted. The symptoms of this condition subsided and recurred frequently until November, 1912, when he presented himself for treatment. The Wassermann test was positive and he was given 0.6 gm. salvarsan intravenously. This was followed by a long-continued administration of mercury proto-iodid and potassium iodid. (It is not known how faithfully this treatment was taken). The Wassermann test was again positive in December, 1913.

The mother is of the same race as the father and is 21 years of age. She was admitted to the maternity wards of Ancon Hospital, Oct. 23, 1913. This visit occurred fifteen months after her marriage and was induced by the advanced stage of her first pregnancy and an associated eclampsia. Her delivery was accomplished by a cesarean section which was performed shortly after her admission. She and the child were both discharged at the end of twenty-three days, both apparently well.

The baby was readmitted at the age of 2 months. It had been nursing and in addition, feedings of a condensed milk mixture had been provided twice daily. The mother had noticed for a week prior to admission that the child had a fever, cold in the head, diarrhea and bloody discharge from the nose. During this time it had also refused to nurse.

Physical Examination.—There was a serosanguineous discharge from the nose and marked embarrassment to nasal respiration. Fissures had formed at the corners of the mouth, nose and eyes, and there was puffing of the hands, feet and face. The soles, palms and mucous membranes were quite pale and an exfoliative change in the skin over the dorsum of the feet and hands left denuded areas between the fingers and toes, from which oozed a thin pink serum. The gums were swollen and bleeding. The superficial sets of lymph-nodes were everywhere somewhat enlarged. Râles could be heard over any part of the chest. The size of the liver, spleen and kidneys could not be determined on account of the protuberant tympanitic abdomen. Blood-films failed to reveal malarial parasites.

The temperature ran an average course of about 100 degrees, the pulse averaging 132, and respirations 36. The child died twelve hours after its admission to the hospital. The clinical factors present and the father's known condition led to the diagnosis of congenital syphilis.

Anatomical Report.—Autopsy 3763. Performed three hours and twenty minutes after the death of the child. It was a plump brown baby showing no developmental variation on external examination. There was slight puffing of the face and the dorsum of the hands and feet. The pale conjunctiva and skin indicated a severe degree of anemia. The abdomen was protuberant and there was some pouting of the umbilical stump. A paper-like exfoliation of the skin was noted over each malar region, the dorsum of the hands and wrists, and over the feet and ankles. A thin pink serum exuded from such denuded areas. A maculopapular eruption similar to that observed in the secondary skin lesions of acquired syphilis was found over the anterior and external surface of the thighs. At the corners of the mouth and nose and eyes and about the vulva were oozing fissures and collections of dried serum scales. The nasal, buccal, vaginal and rectal mucosa revealed a congested fissured membrane but no "mucous patch" was observed. A copious serosanguineous nasal discharge was noted, and this was also present to a less degree from both eyes and the right ear. A gum-like exudate was found plugging the canal of the left ear.

Head Section: A firm chalk-white brain was present with no very noticeable increase in the cerebrospinal fluid. No gross focal lesion noted in brain or skull. The right middle ear contained a thick pink serum.

Neck and Mouth: The lymphatic glands were large, pale structures without evidence of focal necrosis or abscess formation.

Thorax: The costochondral junctions of the ribs presented no marked enlargement. The contour of the chest was normal. A small, pale thymus

gland was present, regular in outline and showing no gross lesion. The lungs were bluish-white in color and air-filled except for a few coin-shaped hemorrhagic areas in the visceral pleura about 12 mm. in diameter. The consistency of the pulmonary tissue beneath these areas suggested small consolidation. The heart was a pale-yellowish structure and the epicardium presented a gelatinous appearance. The muscle seemed friable when handled. Foramen ovale present. Slight increase in pericardial fluid. No focal lesions observed. Aorta: This vessel and its large branches were filled with an almost transparent thin watery blood without extensive clot formations. The intima revealed a few tiny points of degeneration in the thoracic portion of the vessel.

Abdomen: The peritoneum was moist and pale but otherwise normal. All glands were slightly enlarged and pink and showed no focal change.

The esophagus, stomach and duodenum revealed no gross lesion.

The pancreas was almost snow-white but it failed to present gross evidence of a lesion.

Intestine: Some reddening in the mucous membrane of the cecum, sigmoid and ileum (the dependent portions). No lesion and no parasite present.

Liver: Some enlargement. The dome of the right lobe was reddish-brown in color while the anterior margin was marble-white, and the consistency so increased that a uniform gummatous process was strongly suggested. This marginal zone extended backward into the right lobe for fully 2 cm., but showed none of the circumscribed peculiarities of the usual gumma. On section this process was found to extend in a lace-like pattern throughout the right lobe. The gall-bladder and ducts appeared normal.

Spleen: Somewhat enlarged and semisolid. Malpighian bodies quite prominent.

Kidneys: Enlarged and showed decided fetal lobulation. The yellowish color and friable tissue was similar to that found in the heart muscle.

Pelvic Organs: Normal.

External Genitalia: No additional note.

Smears were made from selected tissues which yielded the following results: Smears from blood of jugular vein were stained with a polychrome stain (Hastings). There was evidence of a severe degree of secondary anemia and a lymphocytosis of 56 per cent. was present. The lymphocytes were nearly all of the small type. Attention was arrested by the presence in almost every field of from one to three or more treponemas with the characteristic morphology of *T. pallidum*.

Similarly stained smears from the liver near the gummatous-like region revealed the same organisms in fair numbers. A more protracted search in smears from spleen and bone-marrow and lymph-nodes resulted in sparse findings of the same nature. A Wassermann test on the cadaver was obtained and found positive. Weights of the organs may be grouped as follows:

| | | | |
|------------------|---------|-----------------------|--------|
| Brain | 380 gm. | Combined kidneys..... | 55 gm. |
| Liver | 190 gm. | Spleen | 55 gm. |
| Right lung | 25 gm. | Heart | 20 gm. |
| Left lung | 25 gm. | Thymus gland | 5 gm. |

Microscopical Report.—Skin: This specimen was taken from the anterior surface of the right thigh and although no variation in its histology was noted in the sections stained with hematoxylin and eosin, yet in Levaditi preparations *T. pallidum*, in fair numbers, were found in focal manner in the superficial layers of the corium.

Brain: No lesion was found in any of the preparations. After a tedious search over many specimens of Levaditi preparations a few forms were found which faithfully represented *T. pallidum*.

Noguchi's² identification of this organism in the brain in cases of general paralysis made it seem quite likely that this case of congenital syphilis would easily reveal the presence of *T. pallidum* in fair numbers.

Lymph-Node: A specimen from a set near the liver was chosen for examination and the Levaditi preparations after an extended search revealed a few treponemas.

Heart: A more or less general and moderate fatty metamorphosis was present with no tendency anywhere to focal lesions of any character. Warthin's³ reports (on localization of *T. pallidum* in the heart muscle) stimulated our interest in the Levaditi preparations and many slides were carefully searched. It was disappointing to find these preparations of the heart among the most difficult in the body in our case in which to locate the organism. There was no relation between those found and a focal lesion or perivascular space.

Aorta: Levaditi preparations made from the regions containing tiny points of degeneration in the intima as well as sections from the arch of the vessel and elsewhere failed to reveal any of the organisms.

Liver: Sections from the dome of the right lobe were not far from normal. They simply presented the findings of a fatty change and a moderate round cell infiltration of the perilobular regions.

Sections from the gummatous-like margin showed almost complete destruction of the liver tissue. Columns of cells had been apparently obliterated except for little collections of one or more cells so distorted that the first impression was that of extensive giant cell formation. The new tissue, causing the compression and obliteration mentioned, appears to be a fibrogelatinous network filled with plasma cells. Here and there large areas of focal necrosis had occurred. Levaditi preparations from these regions would show at times a large network of treponemas covering several fields and then several fields might occur before any could be found. There was a more decided tendency in the liver for the coincident finding of a focal lesion and numerous organisms than in any other viscus. It is a noteworthy fact, however, that focal lesions (even in the liver) did occur without the organism being identified in or near the lesion, and on the other hand a rather plentiful finding of the organism was noted in other parts of the liver where no histologic change could be detected.

Kidneys: A general fatty change was noted and in addition many small areas of degeneration appeared which were not recognized grossly or in the hematoxylin and eosin preparations. Many times only a bare outline of a tubule remained. Very infrequently a degenerative glomerulitis was found. Here, also, the treponemas were to be found with or without the presence of a focal lesion. They seemed prone to live in the periphery of the tubules.

Pancreas: A marked interlobular change was found in the head of this organ showing the same type of fibrogelatinous material filled with plasma cells that was present in the margin of the liver. Infrequent focal degeneration was found throughout the organ. Treponemas were occasionally found in colonies but not with the frequency observed in the liver and kidneys.

Spleen: In a few instances central necrosis of malpighian bodies was apparent. Treponemas were found only in sparse numbers. The thymus gland and lungs revealed infrequent *T. pallida*. They appeared in the lung in the small consolidations noted beneath the visceral pleura. The pituitary gland, ovary,

2. Noguchi, H., and Moore, J. W.: A Demonstration of *Treponema Pallidum* in the Brain in Cases of General Paralysis, Jour. Exper. Med., 1913, xvii, 232.

3. Warthin, Aldred Scott, and Snyder, E. J.: Localization of *Spirochaeta Pallida* in the Heart Muscle in Congenital Syphilis in the Absence of Histologic Lesions or of *Spirochetes* Elsewhere in the Body, Jour. Am. Med. Assn., March 9, 1912, p. 689.

uterus, adrenal body, voluntary muscle and aorta failed to reveal any of the organisms after a prolonged search in Levaditi preparations. Some peripheral blood-smears that were made about twelve hours before the death of the child had been stained by Hastings' polychrome method; after these were overstained with Giemsa a tedious search was made for *T. pallidum* without finding any of them. This fact, in connection with their presence in the post-mortem peripheral blood less than four hours after death, is of interest.

It is pretty well established that these organisms prefer the lymph-stream or the sluggish channels of the blood-forming organs, yet at times they have been reported in the blood and in the peripheral blood of cases other than this type. Levaditi⁴ found one positive blood in six cases of general paralysis. It would seem that in cases in which it can be found in the blood-stream, it should be found in a uniform manner throughout all the viscera, yet the study of this case revealed the focal distribution already noted, the liver disclosing the greatest number, then the kidneys, blood from the jugular vein, pancreas, skin and lungs in the order named, while the other organs yielded sparse findings or none at all. Pearce⁵ states that of all the organs in the infected animal capable of transmitting the disease, infection follows most frequently after inoculation with the bone-marrow, the spleen, the lymph-nodes and the testicle, in the order named. It is interesting to note in connection with this statement that the treponema was found in stained smears made at autopsy from rib-marrow, splenic pulp, crushed lymph-node near the liver and from the peripheral blood, but the organisms were found with ease in these tissues only in the smears made from the peripheral blood.

Dr. Darling has suggested that, during the last few hours of life and the few hours intervening between death and the autopsy, the blood had lost to a great extent its normal amount of oxygen, and that this condition favored the presence and rapid development of *T. pallidum* in the venous blood-stream. This appears to be a logical explanation of the apparent absence of the treponemas in the smears of the peripheral blood twelve hours before death. The irregular manner in which they appeared in Levaditi preparations made from the various tissues is also thought by him to be due, in part at least, to the inability of the silver to impregnate the tissue in an even manner or to some characteristic of the parasite or the tissue about it which would not allow it to assume its proper relation to silver impregnation.

This case presents one instance in which, at present, all the conditions conform to Colles' law. The mother at the time of the death

4. Levaditi, C.: Presence of the *Spirochaeta Pallida* in the Blood of General Paralytics (abstr. in Paris letter), Jour. Am. Med. Assn., Dec. 13, 1912, p. 2170.

5. Pearce, R. M.: The Wassermann Reaction in the Pathology, Diagnosis and Treatment of Syphilis. Arch. Int. Med., November, 1910, p. 480.

of the child and again six months later reacted in a negative manner to the Wassermann test performed by Dr. L. B. Bates according to Noguchi's modification of the test. Pearce⁶ claims that it has always been a question whether immunity is real or whether the mother is so lightly infected as to present none of the actual manifestations of the disease. At present, the mother has failed to present any symptoms of the disease while the father continues to respond in a positive manner to the test.

De Buys⁷ has found the mother so frequently positive to the Wassermann test that he recommends its application to the mother's blood when a suspected case of congenital syphilis is under discussion and it is found impossible to apply the test to the child.

6. Pearce, R. M.: The Wassermann Reaction in the Pathology, Diagnosis and Treatment of Syphilis, *Arch. Int. Med.*, November, 1910, p. 504.

7. De Buys, L. R.: A Study of the Wassermann Reaction in Connection with Hereditary Syphilis, *Am. Jour. Dis. Child.*, January, 1913, p. 65.

THE VOICE SIGN IN CHOREA—TECHNIC OF ELICITATION

STUDIES IN NEUROLOGIC TECHNIC NO. 3*

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Previously¹ a preliminary note has been published on the voice sign in chorea, and following that a further study² of this sign in a series of cases.

As a number of requests have come, since these publications, for the technic of elicitation employed to find this sign in the voice, I therefore present here briefly the method used.

TECHNIC

The patient is allowed to sit or stand easily. The purpose is to obtain a fair amount of body relaxation. The operator, as an example to the patient, takes a deep inhalation and sounds for from fifteen to twenty seconds the vowel "a" as in "are." Then instruction is given to the patient as follows: "Do that." This is an easy method to elicit the imitation of a prolonged vowel sound. If merely instructions are proffered they are usually not at first understood, and so it takes quite a time to explain a long breath, a prolonged tone and just the exact tone desired. All this time and trouble is saved by the examiner's performance of the sound desired and trusting to imitation to bring the product desired.

The operator should then watch the sound produced and note any variation in it caused by the choreic contractions. If during this prolongation of "a" as in "are" a contraction occurs in the expiratory muscles, the sound will markedly change in intensity and for the rest of the utterance, or until the occurrence of another contraction, the

* Submitted for publication Nov. 28, 1914.

* Studies in Neurological Technique, No. 1: The Points in Jendrassik's Method of Eliciting the Patella Reflex, *Alienist and Neurologist*, 1913, xxxiv, No. 3.

* Studies in Neurological Technique, No. 2. Indication and Method for the Use of Electrical Reinforcement for the Elicitation of Absent Reflexes, *Rev. Neurol. and Psychiat.*, January or February, 1915.

1. Swift, Walter B.: A Voice Sign in Choreia, *AM. JOUR. CHILD. DIS.*, June, 1914, p. 422.

2. Swift, Walter B.: Further Analysis of the Voice Sign in Choreia, *AM. JOUR. CHILD. DIS.*, October, 1914, p. 279.

sound will return to its previous evenness of utterance. If during the sounding of "a" there occurs a choreic contraction in or near the vocal cords so that they are made more tense, the tone of that sound of "a" is thereby raised in pitch and then resumed at its previous level.

The test may have to be applied four or five times before the voice sign shows. Sometimes it occurs the first time tried and regularly every time. Rarely ten trials are necessary. The typical choreic voice sign is a change in pitch and intensity. "A" is chosen for the clinical test because the mouth and passages are more easily touched by choreic contraction if widely opened than if constricted.

I shall be glad to hear from others who find this sign present.³

SUMMARY

The technic for eliciting the voice sign in chorea is to request the patient to sound a prolonged "a" as in "are" and to watch for the changes in vocal pitch and intensity which constitute the sign.

110 Bay State Road.

3. To any who would like reprints of the articles mentioned above, they will be mailed on receipt of address.

BOOK REVIEW

SÄUGLINGERNÄHRUNG UND SÄUGLINGSTOFFWECHSEL. EIN GRUNDRISS FÜR DEN PRAKTISCHEN ARZT. Von Leo Langstein und Ludwig F. Meyer, Verlag von J. F. Bergmann, Wiesbaden, 1914.

After an interval of four years we have a second edition of this excellent work on the feeding of infants. The book now comprises four hundred instead of two hundred pages. Its scope, however, is the same and includes a consideration of milk from a chemical, physical and caloric point of view, the feeding of the breast-fed and bottle-fed infant, and a detailed analysis of the symptomatology of the various nutritional disturbances which occur during the first year of life. Throughout, Finkelstein's clinical point of view is maintained and his classification of intestinal disorders is the one that has been adopted. The book has been enlarged so as to include the latest researches in the physiology and pathology of pediatrics and there is no other single volume in any language which covers the field so completely. Although the reader may differ with some of the authors' conclusions, there can be no criticism on the ground of lack of care or thoroughness in the preparation of this work. It is a book which should be read carefully by all those who are especially interested in pediatrics and, although it may be found to be too specialized for the general practitioner, its pages will no doubt prove suggestive to those who are actively interested in the nutritional diseases of adults.

A. F. H.

PROGRESS IN PEDIATRICS

RÉSUMÉ OF WORK ON TUBERCULOSIS IN CHILDREN FOR 1914

MAY MICHAEL, M.D.
CHICAGO

PORTALS OF ENTRY

1. Von Pirquet: Bronchogenous, Placentogenous, Dermatogenous, Enterogenous Infection with the Tubercle Bacillus, *Edinburgh Med. Jour.*, 1914, xiii, 220.
2. Jousset, A.: Portals of Entry of Tuberculous Infection, *Pédiat. prat.*, 1914, xii, 208.
3. Moeller, W.: Congenital Tuberculosis, *Arch. mens. d'obst. et de gynéc.*, July, 1914.
4. Scheltema: Tuberculous Infection in Infants, *abst. Jahrb. f. Kinderh.*, 1914, lxxx, 118.
5. Chancellor, P. S.: Contribution to the Study of the Primary Lesion in Tuberculosis, *Ztschr. f. Kinderh. (orig.)*, 1914, x, 12.
6. Wollstein, M., and Bartlett, F.: A Study of Tuberculous Lesions in Infancy and Young Children, Based on Post-Mortem Findings, *AM. JOUR. CHILD. DIS.*, 1914, viii, 362.

Von Pirquet¹ discusses the portals of entry of the tubercle bacillus in infancy. He finds fetal transmission very rare. Sometimes infection takes place through the placental blood-vessels and sometimes by aspiration of the amniotic fluid. Placentogenous infection causes no primary lesion. Post mortem the lymphatic nodules in the liver and adjacent parts show the most advanced lesions. Clinically, new-born infants infected with tuberculosis are under weight and begin to waste away. Fever and meteorism develop and sometimes tuberculids on the skin. The lungs remain free of symptoms. The prognosis is absolutely bad.

Primary infection of the intestinal canal in infants has been much overestimated. Intestinal lesions are a common finding post mortem, but are as a rule secondary, because of the deglutition of tuberculous mucus from the lungs. There is no characteristic clinical picture of primary intestinal tuberculosis. General atrophy with a large abdomen has been found, but the cases with post-mortem proof of primary intestinal infection are not numerous enough to permit any statement as to the symptoms.

Primary infection of the mucous membranes is also rare. Against the view of those who held that the tonsils were a frequent portal of entrance are the statistics of Albrechts, who found only three instances

of primary tonsillar infection in 1,060, about 0.3 per cent., and those of Ghon, who found one instance in 189 cases, or 0.5 per cent. The primary lesion shows ulceration and the regional lymphatics are intensely swollen.

A few cases of primary infection of the skin are reported; one of these is that of Chancellor, who cared for a 2-months-old baby with a lesion on the cheek, where she was bitten by a tuberculous nurse.

In the first years of life there is no doubt that the bronchogenous mode of infection is the most frequent. Von Pirquet estimates that in 95 per cent. of the cases this is the route of infection.

A. Jousset² is of the opinion that the chief portals of entry for the tubercle bacilli are the upper parts of the digestive and respiratory tracts, namely, the mucous membrane of the nose, throat and tonsils. He thinks it probable, however, that the tubercle bacilli can enter through the mucous membrane of the genitalia and that the greater frequency of tuberculous peritonitis in the female sex bears a relation to vulvovaginitis, caused by the tubercle bacillus.

Of interest also is the report of the writer infecting himself with virulent tubercle bacilli of the bovine type through a small wound on the finger. A few days afterward there appeared a small tuberculous nodule with swelling of the axillary lymph-glands. Later there was swelling of the bronchial glands and mild pulmonary disease.

Scheltema⁴ emphasizes the great danger for infants of tuberculous infection and reports two cases in which it is his opinion that the infection took place through the skin. The first child was admitted to the hospital at the age of 8 weeks with a tuberculous ulcer on the forehead. He had had a small wound on the forehead and had been cared for by his tuberculous father who expectorated a great deal. The regional lymph-glands were swollen. The child died one year later of a generalized tuberculosis.

The second child had three tuberculous skin ulcers on different parts of the body. For two weeks he had been cared for by a tuberculous woman. Necropsy showed pulmonary involvement with cavity formation.

M. Wollstein and F. H. Bartlett⁶ have made a study of the tuberculous lesions found post mortem in 178 infants and young children. The children varied in age from 2½ months to 5 years, and 75 per cent. were under 2 years. The classification was made whether the lesions in the lungs and bronchial lymph-nodes predominated, or whether the ones in the intestinal tract and mesenteric nodes were more marked. In five cases of the first or pulmonary group the tuberculosis was found limited to the bronchial lymph-nodes, and in all five the lesion was an active one; in two cases the tuberculosis was limited to one

lung and adjacent lymph-nodes, in one case to the bronchial lymph-nodes and pia mater, in one to the bronchial nodes and fingers (dactylitis). In the greatest number of cases (135) the tuberculous lesion of the lungs and bronchial nodes were the oldest lesions of a generalized infection.

In one case of the second or intestinal group, the lesion was limited to the mesenteric lymph-nodes, in one to the intestine and the mesenteric and cervical lymph-nodes. In fifteen cases the tuberculous lesions of the intestines and mesenteric glands were the most advanced lesions of a more or less generalized infection.

There were only fourteen cases in which the lungs were not involved, and only nine in which the bronchial lymph-nodes contained no evidence of tuberculosis. The mesenteric glands were less frequently involved than the bronchial glands. Tuberculous meningitis occurred in sixty-nine cases, in fifty of which the children were below 2 years of age.

A study of the lesions showed that there was a marked tendency to rapid and general dissemination of the tuberculous lesions throughout the body in infants less than a year old. In the entire series not a single healed tuberculous lesion was encountered, and attempts at healing, shown by calcified areas, were found only five times in the lung and thirteen times in lymph-nodes.

The largest number of cases was evidently of inhalation origin, as in most instances the pulmonary lesions were the most advanced in the body. The presence of tuberculous areas in the bronchial glands in seven instances, when there was no pulmonary involvement, seems to show that it is possible for the tubercle bacilli to pass through the lungs without localizing there. Wollstein and Bartlett prefer this explanation of the absence of the pulmonary lesion in the presence of a bronchial gland tuberculosis to that of Ghon, who believes that the pulmonary lesion is always present and, where not found, is merely overlooked.

The smaller proportion of cases of tuberculous meningitis among children who acquire tuberculosis by ingestion, as compared with those who become infected by inhalation, is in keeping with the fact that the deglutition cases show rather less tendency to generalization than do the respiratory cases.

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18. Mandlebaum: Changes in the Cerebrospinal Fluid in Tuberculous Meningitis, *Deutsch. Arch. f. klin. Med.*, 1914, cxiii, 92.

A. Philip Mitchell has made a study of cervical gland tuberculosis among the children of Edinburgh because the disease is frequent in this locality and because little attention has been paid to it.

His investigations included seventy-two consecutive cases. Cervical glands excised at operation were received in sterile gauze and inoculated into guinea-pigs and the lesions which subsequently developed were the immediate source of culture. Mitchell also attempted to find a relation between clinical data and milk-supply. He found that in 90 per cent. of the cases the bacillus was of the bovine type and that milk containing the bovine tubercle bacillus was clearly the source of infection. A very important fact brought out by the study was that 84 per cent. of the children, 2 years of age and under, had since birth been fed unsterilized cow's milk. Mitchell thinks that emphasis on the human sources of infection has blinded us to the fact that the drinking of milk is an important factor in the infection of children with tuberculosis. He feels that the tonsils are the most important portal of entry for the tubercle bacillus. The high percentage of tonsils in which the bovine virus was present is further proof of the frequency of tuberculous cow's milk as a source of infection.

N. Raw,¹⁹ after making an extensive study of the subject of human and bovine tuberculosis, adheres to the view he previously published, that man is attacked by two distinct types of tuberculous infection, one conveyed by a tuberculous person, the human type, and the other by infected milk or meat, the bovine type. Primary pulmonary phthisis seems to result from inhalation of the human bacillus and tuberculous ulceration of the intestine to result secondarily from the swallowed sputum. Tuberculous cervical adenitis, peritonitis, joint disease, and probably meningitis and lupus are caused by the bovine bacillus, absorbed from the digestive tract. While the human bacillus produces ulceration of the intestine, the bovine type passes through the intestinal wall and attacks the mesenteric glands, whence the infection spreads

to the lungs. The cervical glands may become infected from the tonsils, the bacillus being conveyed to them directly by the milk. The infection may remain limited to the glands, or spread downward and cause an extensive bovine infection of the lungs.

Raw has instituted inquiries in a number of foreign countries where there are no tuberculous cattle or where cow's milk is not drunk by children and has ascertained that in these countries surgical forms of tuberculosis do not exist, while phthisis is frequent. He ascertained also that in England during the last fifty years there is a marked diminution of phthisis (45 per cent.), while abdominal tuberculosis in children has increased and, what is more significant, tuberculosis in English cattle has rapidly increased. During the last five years Raw has never seen a case of *tabes mesenterica* in which cow's milk had not been given for several weeks or months.

Raw has also come to the conclusion that the two forms of tuberculosis are antagonistic in the human body and that children who suffer from the surgical forms are rarely attacked by phthisis. This belief has been substantiated by his necropsy findings.

M. P. Ravenel¹¹ quotes statistics which show that bovine infection is much commoner in younger children than in older ones, and commoner in older children than in adults. He cannot explain the apparent immunity of adults to infection with the bovine germ. He is, however, of the opinion that prolonged residence in the human body can so change the morphology and characteristics of the bovine germ as to make its origin unrecognizable. The type of bacillus, then, which is often isolated from human beings and which presents only the characteristics of the human germ, may in reality be the bovine germ.

Ravenel does not think there exist facts enough to show the relative importance of infection from bovine sources and infection from human sources; still, while it must be conceded that infection from fellow men is the more common source, in children bovine infection is quite frequent. The lesson, he says, to be learned from these facts is that our communities must be served with milk which comes from cows known to be healthy.

H. Beitzke¹² reports in a 14-year-old boy a fatal case of tuberculosis due to the bovine tubercle bacillus. The boy was accustomed to play in the cow-stable and to drink freely of raw milk from infected cows. When seen by Beitzke, the patient had been sick for a number of weeks with indefinite symptoms. He emaciated rapidly and died within six months of the first examination. A necropsy was obtained and a generalized tuberculosis of unusual form and severity was revealed. Beitzke had never before seen such marked caseation of the glands or such large caseated nodules as were found in the spleen and lungs.

The chief seat of the disease was the mesenteric glands and the mediastinal and supraclavicular glands were evidently involved secondarily from these. Animal experiments showed the infecting organism to be the bovine tubercle bacillus.

The case was chiefly reported because of the alleged mildness of infection with bovine tubercle bacillus. From a pathologic anatomic standpoint the case was the most extensive ever seen by Beitzke.

H. Brooks¹³ gives his experience, extending over a period of ten years, with tuberculosis in a herd of 425 Holstein cows. During this time all tuberculous cows were isolated and treated with injections of tuberculin. In the tuberculous herd were born 200 calves, which were taken from the mothers and fed on the pasteurized milk of healthy cows. None of these calves developed tuberculosis; rather they showed a resistance to the disease. Moreover, their development did not suffer.

Brooks deduces from his observations that tuberculosis in the parent has no detrimental effect on the progeny.

T. A. Ossinin¹⁴ adds the following to the subject of latent tuberculosis. Pathologic anatomists declare that latent tuberculosis frequently occurs. Former statistics considered latent only those cases which clinically gave no evidence of tuberculosis, but in which at autopsy tuberculous lesions were found microscopically. There is, however, another form of latent tuberculosis, namely, that in which no lesions can be found macroscopically, but in which injection of the lymphatic glands into guinea-pigs gives rise to a tuberculosis.

Ossinin examined 100 cadavers of children who had shown no evidence of tuberculosis during life. In 97 per cent. there was also at necropsy no evidence of the disease macroscopically; no tubercle bacilli were found in the lymphatic glands, and tuberculosis did not develop in guinea-pigs injected with the glands. In three cases, in spite of the fact that no gross tuberculous lesions could be found, tubercle bacilli were found in the glands by the antiformin method and tuberculosis developed in guinea-pigs injected with the glands. In two of these three cases the tubercle bacilli seemed non-virulent, as only local lesions developed; in one there was a generalized tuberculosis. In all three cases the tracheobronchial glands were the ones affected, and Ossinin thinks that this perhaps substantiates the theory that the respiratory organs are the chief portal of entry for the tubercle bacilli.

The great difference in the reports of various authors regarding the presence of tubercle bacilli in the blood-stream led P. Lehnmann¹⁵ to make a study of the subject. Thinking that reliable results could not be obtained from blood-smears, he limited himself to animal experiments. The blood of 140 children was studied, but the results in thirty-

six cases were excluded because of the possibility of error. The blood was obtained from the vein at the elbow, diluted with normal salt solution, and injected into the peritoneal cavity of guinea-pigs. In only six instances did the animal develop tuberculosis.

Lehmann does not believe that the acid-fast bacilli so often found in blood-smears of patients suffering from tuberculosis are tubercle bacilli, or that any diagnostic or prognostic significance can be attached to their presence, because, in the first place, the animal experiments showed them so seldom (six out of 104 cases) and, in the second, in meningitis and generalized tuberculosis in which the bacilli might be expected, the experiments were negative.

Mandelbaum¹⁸ found that in tuberculous meningitis the lumbar fluid, which before death is clear and transparent, becomes decidedly cloudy. This cloudiness is due to large mononuclear cells which are macrophages and probably originate in the endothelium of the meninges. They contain lymphocytes, polymorphonuclear cells, and often tubercle bacilli. They are also the bearers of a proteolytic ferment, which accounts for the increase after death in the proteolytic index of the lumbar fluid.

DIAGNOSIS

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J. B. Hawes¹⁹ discusses the conditions under which the diagnosis of tuberculosis in children is justified. A bad family history and history of exposure are important factors, but the absence of both does not preclude a positive diagnosis. Length and intimacy of exposure are important. A diagnosis of tuberculosis is rarely justifiable, unless constitutional signs and symptoms are present, in spite of what the Roentgen ray shows. As regards local signs and symptoms, cough and expectoration have many causes besides tuberculosis. Marked dulness and râles are significant. The detection of finer shades of dulness, the significance of harsh or puerile breathing, prolonged high-pitched expiratory sounds, bronchial whisper voice, and paravertebral dulness require long experience to interpret properly. D'Espine's sign simply suggests that something is present which transmits the whispered voice sounds from the trachea through the dorsal vertebra at a lower level than in normal children.

Roentgen ray is of value only in conjunction with other features.

A negative tuberculin test, if carefully performed and confirmed by a subsequent negative test, is as good evidence as possible that tuberculosis can be ruled out. A positive test is not so conclusive, but is confirmatory evidence.

P. Van Pée²¹ thinks that the so-called orthopercussion of Goldschneider is one of the most valuable aids for diagnosing tuberculosis in infants. To obtain results percussion should be practiced as lightly and over as limited a space as possible, by placing the finger vertically on the chest and percussing the distal phalanx. Practiced in this way, percussion shows that the two lungs react differently to microbic infections. The left lung reacts first and returns more quickly to normal. Signs in the right lung appear later and have a tendency to persist.

This difference is explained by the greater vascularity of the left lung caused by the proximity of heart and large blood-vessels.

According to Van Pée, most pediatricians believe that tuberculosis in the infant is a latent process, which progresses rapidly toward a fatal termination. He, however, believes that it can in the majority of cases be detected and that it runs a chronic course as in the adult.

D. B. Lees²² believes that it is not only possible but even easy to establish a diagnosis of chronic pulmonary tuberculosis in children by inspection, palpation, percussion and auscultation, provided these procedures are carefully and methodically carried out. In order properly to percuss the chest, all muscles must be relaxed and adequate counter-resistance provided for, and this can be obtained for the front of the chest only when the patient is lying down. For examination of the back of the chest the sitting, slightly stooping posture should be assumed with the hands on the anterior aspect of the opposite shoulders and the elbows near to each other. Careful percussion will then reveal small areas of incipient tuberculosis in children, even when the Roentgen-ray photographs show little or nothing. Percussion will also demonstrate large areas in cases in which there are few or no morbid sounds audible.

It appears to Lees that accurate percussion is of primary importance in the diagnosis of pulmonary tuberculosis both in children and in adults, and that it is capable of revealing the disease at a much earlier period than is possible by any other method of investigation.

E. Rach²⁴ describes the Roentgen-ray pictures which correspond to the various anatomic types of tuberculosis in children.

Ghon's Primary Lesion: A diagnosis of Ghon's primary lesion can be made with all probability in children giving a positive von Pirquet reaction, if a sharply defined bean-sized shadow is found isolated and free in the pulmonary field and if at the same time the picture shows enlargement of the bronchial glands draining this area. If Ghon's lesion lies near the hilum, it cannot with certainty be differentiated from hilum glands.

Intumescent Tubercular Bronchial Glands: By intumescent glands, Rach means those sufficiently large to cause pressure on the neighboring lung tissue. The right upper bronchial glands show most frequently in Roentgen-ray pictures. They produce a shadow to the right of the median shadow, the convexity extending upward, then running parallel to the median shadow, finally turning backward, and again joining the median shadow.

Intrapulmonary Hilum Tuberculosis: Anatomically, this form consists of caseated intrapulmonary glands in the neighborhood of the hilum and caseated areas, extending laterally from the hilum in streaks.

The caseated areas often break down and form cavities. The Roentgen ray gives a definite shadow extending from the median shadow, more often to the right than to the left, into the pulmonary field. It becomes less thick and loses its sharp outline at its periphery. Its upper and lower borders show pointed processes.

Miliary Tuberculosis: Often Roentgen-ray findings give evidence of disease weeks before there are clinical symptoms.

Phthisis of Infants: Anatomically, this type is characterized by numerous areas of caseous pneumonia, often with cavity formation. The Roentgen-ray picture shows wide-spread shadows whose borders are limited by the borders of the lobes. Within these shadows are sharply defined light areas (cavities). Enlarged glands are also seen.

Apical Tuberculosis: Roentgen pictures of this form are identical with those of apical tuberculosis in adults.

According to W. P. Northrup,²⁵ two reliable aids in the diagnosis of miliary tuberculosis are the Roentgen-ray apparatus and the presence of skin eruptions. Cases of miliary tuberculosis present to the experienced observer the mental picture of pneumonia but the physical signs of bronchitis, and at this point the physician may be unable to procure any reliable testimony for exact diagnosis until a good Roentgen-ray picture has been procured. Next to necropsy, Northrup thinks the Roentgen ray gives the most intimate knowledge of the lesions in the child's lungs.

Eruption of miliary tubercles furnishes a pathognomonic sign for diagnosis and a valuable, almost conclusive, point for prognosis; that is, the lesion is nearly always associated with a fatal form of tuberculosis in the young child. Among the characteristics of the individual lesions may be mentioned that in size it is like a rose spot in typhoid fever, topped by a tiny vesicle, surrounded sooner or later by a congested or hemorrhagic zone with the formation of a crust, which when removed, leaves a little pit.

According to W. I. Bruce,²⁶ fine detail is absolutely necessary for the recognition of tuberculous infiltration by the Roentgen ray, and this can be obtained only by employing photographic methods. In Roentgen-ray screens there can be seen limitation of movement of the diaphragm on the affected side, increased opacity and general elongation of the cardiac opacity. Skiagrams show increased opacity of the affected lung, somewhat striated in arrangement and also made up of small rounded opacities arranged in groups. In cases of chronic tuberculosis of the lungs when the infiltration is dense, the small rounded opacities overlap and larger patches result. When lung tissue has been destroyed and cavity formation has occurred, there occur areas of great translucency, usually surrounded by densely infiltrated lung tissue.

W. J. Dodd,²⁷ in discussing the value of the Roentgen ray in the diagnosis of tuberculosis, says that, if a pathologic lesion is present, the Roentgen ray will always reveal it. But it must be clearly understood that a lesion is not necessarily a tuberculous one because revealed by the Roentgen picture. The Roentgen picture is a projection picture and a record of density, and any lesion that will cause increased density will present a departure from the normal.

Recently Dodd made Roentgen-ray examinations of the chests of 100 children. A careful physical examination and every effort to determine the presence of tuberculosis had been made by the pediatricians before the patient was referred for a Roentgen-ray picture. In all instances in which there was clinical evidence of a lesion this was confirmed by the Roentgen picture. In several instances lesions were found which were not made evident by clinical examination. In only seven cases was there evidence of active disease, yet eighty-nine showed some pathologic lesion in the Roentgen picture. The report in the great majority of the cases was enlarged hilum and peribronchial glands. The results in this series show that other conditions besides tuberculosis will reveal evidence of enlarged hilum and bronchial glands, and emphasize the great importance of a complete examination before a diagnosis of tuberculosis is made. A diagnosis of tuberculosis should not be made until positive clinical evidence is obtained. Repeated Roentgen examinations at intervals of a month or less are advisable. By this means it is frequently shown that the lesion has cleared up, and this would not be the case if lesions were tuberculous.

G. Bessau and J. Schwenke²⁹ wished to ascertain whether an increase or decrease of sensitiveness to repeated doses of tuberculin has diagnostic or prognostic significance. One hundred and fifty-three children of the polyclinic were used for the tests, but twenty-four were excluded because in them the tests were always negative. Three strengths of tuberculin were used: 1:10,000, 1:1,000 and 1:100. In the first test 0.1 c.c. of the weakest solution was injected intracutaneously into the extensor surface of the thigh. The size of the reaction was noted after twenty-four, forty-eight and seventy-two hours. Eight days after the first injection the second was given in the corresponding place on the other thigh. If the first reaction was positive, the weakest solution was used again; if negative the next strongest solution was injected. If the second reaction was negative, a third injection of 0.1 c.c. of the 1:100 solution of tuberculin was given.

The results show that in clinically manifest tuberculosis there is no tendency to an increase of the local tuberculin sensitiveness, while in individuals in whom tuberculosis is latent this always occurs. An

increase of local sensitiveness in cases of active tuberculosis means that the prognosis is favorable.

Bessau and Schwenke also make the following observations from their tests: In childhood a marked local tuberculin reaction following an injection of 0.1 c.c. of a 1:10,000 solution usually indicates an active process; a very marked reaction is usually a good prognostic sign. Weak reactions may signify the presence of a progressive or a latent process. In these cases a repetition of the test is of especial value. Marked increase in the reaction excludes a progressive process.

J. Cronquist³⁰ made some interesting observations on the von Pirquet test in children with exudative diathesis and in children without this taint. He vaccinated forty-two children daily for from two to four weeks. After twenty-four hours he measured the size of the papule and made a curve of the results. In children not suffering from an exudative diathesis the papules were at first irregular, increased in size for ten or twelve days, then decreased slightly, so that at the end of two weeks they were all practically 10 mm. in diameter. In children with an exudative diathesis, the papules were always larger than in those of the first group. There was decided variation in their size from day to day and this lasted as long as the children were revaccinated.

Cronquist also performed experiments to ascertain whether the blood-serum of children who had been treated with tuberculin, when mixed with tuberculin, had any effect on the von Pirquet reaction. In some instances he inactivated the serum before mixing it with the tuberculin. These experiments showed that no marked difference existed between active and inactivated serum; that no difference in the von Pirquet test was obtained, when serum from children receiving less than 0.059 gm. of tuberculin was used, but that when the blood-serum came from children receiving more than 0.20 gm. of tuberculin, there was a decided diminution in the size of the papule. The effect increased with the size of the dose of tuberculin, so that a negative reaction was obtained with blood-serum of children receiving 0.2 to 0.5 gm. This prohibitory effect disappeared only after the tuberculin treatment had been discontinued for some weeks or months.

M. Kasahara³² has made histologic examinations of the papules produced by vaccinating with tuberculin, diphtheria toxin and atoxyl. Macroscopically, these skin reactions are very similar, but histologically, Kasahara found decided differences. The papule resulting from the tuberculin test showed giant cells and infiltration of lymphocytes around the blood-vessels. The giant cells were due to irritation by the tuberculin. The diphtheria toxin papules showed decided changes in the vessel walls. There was thickening of the intima, dilatation and

engorgement of the vessels, and a fibrinous inflammation of the corium. The atoxyl papule showed a somewhat marked lymphatic infiltration into the corium.

Kasahara thinks that this histologic study is proof that the tuberculin reaction is a specific one.

L. Bruce Robertson³³ studied the von Pirquet test in surgical tuberculosis of children, taking his material from 350 cases noted in hospital records of the last four years. Of those showing clinical evidence of tuberculosis, all but 2.9 per cent. gave a positive reaction. In the clinically non-tuberculous cases the reactions were mostly negative. The von Pirquet test, then, may be regarded as specific in cases of surgical tuberculosis; and the fact that it is positive in a moderately small percentage of clinically non-tuberculous children does not outweigh its value as a diagnostic test. There is a much greater proportion of positive reactions in apparently non-tuberculous cases than of negative reactions in those clinically tuberculous.

H. Koch and W. Schiller³⁴ substantiated the findings of a number of observers who found that tuberculous areas in the skin react more violently to the von Pirquet test than normal areas. As tuberculous areas, Koch and Schiller used the sites of former cutaneous or intercutaneous vaccinations. They chose the artificial tuberculous areas because they could control the site of application and apply the test at any stage. Three series of tests were made. In the first the second vaccination was performed during the acute inflammatory process of the first vaccination, and was termed the intrafocal reaction; in the second it was done after the first vaccination had run its course and was termed a scar reaction. In the third series the test was made in the tissues around the primary vaccination area and was designated as a parafoal reaction. The results were interesting. Different results were obtained according to the site of application and stage of primary vaccination. Intrafocal reactions showed no uniform relation to a control vaccination, but it was always observed that the longer the time between the two vaccinations the more marked was the second test. Scar reactions were always more marked than controls made in normal skin areas. The parafoal reactions were only stronger than the controls if the vaccination site was within the area of primary vaccination.

Koch and Schiller give the following explanation of these observations: The specific tuberculin inflammation is an allergic process caused by a reaction between antigen and antibodies. Variation and the quantitative relation of antigen and antibodies cause variation in the intensity of the tuberculin reaction. In the newly inflamed areas there are no free antibodies which can combine with the antigen, but after subsidence of the inflammation there remains an accumulation

of the antibodies so that a second vaccination in this area results in a stronger reaction.

H. Nothmann³⁵ vaccinated a number of children with human and bovine tuberculin. He wished to see whether it could be ascertained in this way which is the infecting organism. Two hundred and seven children from 1 to 16 years of age were tested. Fifty-six, or 27 per cent., did not react to either. In 145 the test was positive, and in 133, or 91.7 per cent., of these it was positive to both tuberculins; in two, or 1.4 per cent., to bovine tuberculin alone; in nine, or 6.2 per cent., to human alone. As the negative test frequently became positive after two or more applications of tuberculin, deductions were never made from one vaccination.

Nothmann does not think this method of any value in determining the variety of the infecting organism. He thinks that only one fact can be gleaned from the tests, namely, that the majority of tuberculous patients react to both human and bovine tuberculin. His explanation is that in both tuberculins are similar groups of reaction bodies, and that the homologous group is stronger than the specific group, therefore, no matter what the variety of infection, a double reaction occurs.

W. Egert³⁶ obtained in children who were suffering from pulmonary tuberculosis or in whom tuberculosis was suspected a strongly positive cutaneous reaction and a negative subcutaneous reaction, when the tests were performed simultaneously. As the children's condition improved he obtained a marked subcutaneous reaction and only a very slight cutaneous reaction. Egert believes that a positive "contrast" phenomenon, as he calls this positive subcutaneous and negative cutaneous reaction, may be of prognostic value, but more observations must be made before this point can be determined.

N. Blumenau³⁹ described a new tuberculin test, which he calls the "plaster test." He cleanses the skin of the forearm with ether, puts a drop of tuberculin on the flexor surface near the fold of the elbow, and covers it with a piece of adhesive plaster, 3 cm. square. The tuberculin must not run over the edge of the plaster and the plaster should be pressed down only around the edge. Sometimes in twenty-four hours, more often in forty-eight, a characteristic eruption appears beneath the plaster. If the reaction is slight the eruption resembles a tuberculid; if marked, it consists of bright rose-red papules, capped with small nodules or vesicles. Blumenau used this test on 227 children and found it very satisfactory, equal to the von Pirquet test in sensitiveness.

J. Müller⁴⁰ reports an instance of gangrene of the nose and other severe results following a diagnostic tuberculin test. The patient was a boy of 15 who suffered from a generalized glandular enlargement.

One drop of a 1 per cent. tuberculin was given intercutaneously for diagnostic purposes. After twenty-four hours there was vomiting, diarrhea and fever. The following day the face was a livid color, and the face, lips nose and neck were swollen. There was a spotted eruption on the trunk. The fourth toe of the right foot and the third toe of the left became gangrenous, as did also the tip of the nose. The mucous membrane of the throat was red and the tonsils were very much swollen. The intercutaneous test was markedly positive.

Müller says that this experience teaches that care must be taken in giving the intercutaneous test when there is a wide-spread glandular tuberculosis.

S. Maggiore⁴¹ bases the following conclusions on many examinations of the blood of children in the various stages of tuberculosis. No stage or form of tuberculosis offers a typical blood-picture. The cases present normal blood findings, diminution of the hemoglobin content and of the red blood-cells; the number of white cells is usually normal or increased, only exceptionally decreased. In infants as well as in older children is found a relative increase in the monocellular element and transitional forms. The basophilic cells are usually decreased or present in normal numbers; the eosinophils are only exceptionally increased. When the hemoglobin and number of red cells are markedly diminished, a polychromatosis and anisocytosis can be demonstrated and exceptionally myelocytes are found.

The changes are undoubtedly due to a specific toxin, but this cannot always be demonstrated. The increase in the mononuclear cells is an expression of reaction on the part of the bone-marrow.

SYMPTOMATOLOGY

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R. Cruchet⁴³ describes the clinical course of tuberculosis in infants. The acute miliary form is rare during infancy. Usually after an indefinite period of anemia, emaciation, vague respiratory signs and persistent cough, suddenly a meningitis develops and death occurs in the course of from eight to fifteen days.

Under the heading of subacute and chronic forms, Cruchet describes several types: the anemic, characterized by marked pallor

and emaciation; the abdominal, with symptoms of a persistent dyspepsia or those of an athrepsia; the respiratory, with persistent dry cough and paroxysms of cough, as in whooping-cough; the glandular, characterized by enlargement of either the mesenteric or the tracheo-bronchial glands, or by a generalized peripheral adenopathy; the cutaneous, with hard nodules in the skin which roll under the examining finger, and over which the skin is brown or violet color (in the later stages these nodules break down and small fistulas persist) and the nervous, characterized by irritability.

With any of these forms it is almost impossible, clinically, to make a correct diagnosis at the onset. Laboratory tests, with perhaps the exception of the tuberculin test, are also discouraging. As the disease advances, however, the symptoms become more characteristic and laboratory tests more useful.

The prognosis of tuberculosis in infants is very grave. Cure is possible, but rarely occurs.

M. Péhu and Mouret⁴⁴ report in a 3-months-old baby a case of generalized tuberculosis, which was interesting not only because of the age of the child, but because of the rapidity of its course and widespread dissemination of the lesions.

The child was born of healthy parents but, when 3 weeks old was given for three weeks in charge of a woman with open tuberculosis. The child began coughing shortly after returning to the parents and, when examined at six weeks, showed symptoms not only of extensive pulmonary involvement, but of meningitis. The face was pale, the head thrown back in position of opisthotonos, there was conjugate deviation of the eyes, the anterior fontanelle bulged, there was marked dyspnea with rapid respirations, 56 to the minute, and cyanosis. Auscultation of the chest revealed scattered mucous râles and tubular breathing at the right apex, where there was also impaired resonance. The liver extended two fingers' breadth below the costal arch and the spleen to the anterior superior spine of the ilium. A small nodular mass could be felt in the epigastrium, a little to the right of the median line. The child died two days after entrance to the hospital.

Necropsy revealed a wide-spread tuberculous process. There were only twenty-four days between the time the child was returned to his parents and the hour of death, and in this interval the bacilli invaded all the organs, lungs, liver, spleen, heart and meninges. In the small intestines were small ulcerations contiguous to the arteries and proving that the infection was hematogenous in origin.

In discussing the mode of infection of infants, Péhu and Mouret mention infection through the placenta, in cases of advanced tuberculosis of the mother (congenital tuberculosis) infection through inhala-

tion of dried sputum from tuberculous parents or, what was evidently the mode of infection in this instance, from a tuberculous caretaker. Careful examination of both parents showed no evidence of infection and the child had never been fed raw milk, so that infection from this source has to be excluded.

J. S. Leopold⁴⁵ reports a case in a 7-year-old child of tuberculosis of the lungs, liver and spleen, with general glandular enlargement. The points of chief interest in the physical examination were the great enlargement of the spleen, the ascites, and the anemia with leukopenia. At necropsy there was found a chronic miliary tuberculosis of lungs, liver and spleen.

Leopold's chief object in reporting the case was to call attention to the difficulty of classification of tuberculosis combined with atypical changes in the lymphatic system. He thinks that there can be no satisfactory classification until the etiology of the affections of the lymphatic system has been determined.

Ribadeau-Dumas⁴⁶ says that cavity formation is not so very rare among children. Among sixty-eight autopsies on children 1 and 2 years old he has found cavities twenty-two times. In eleven cases the cavity was as large as a nut or larger. Clinically, the diagnosis is difficult to make. Ribadeau-Dumas reported the case of a 6-month-old infant who died of a caseous tuberculosis involving the upper left lobe. Clinically, the cavity could not be detected, but in a series of Roentgen-ray pictures, one taken each week, its development could easily be followed.

J. D. Rolleston and J. E. Robertson-Ross⁴⁷ report a case of fatal hemoptysis in a child of 4 years. The child was admitted to the hospital with a paroxysmal cough, which resembled whooping-cough. On examination rhonchi and râles could be heard, but no areas of dulness could be marked out. The abdomen was distended and the superficial veins dilated. Both liver and spleen were enlarged. For two months there was very little change in the child's condition; then dulness was noted below the ninth rib on the left side, extending around into the left axilla. The following week a little blood-stained sputum was expectorated and on the day after a sudden copious hemoptysis occurred, when death almost immediately followed.

At necropsy there were found enlarged and tuberculous tracheo-bronchial glands; the left pleura was thickened and adherent to the chest wall. The upper lobe of the left lung was studded with tuberculous deposits. The lower lobe was solid and presented a cavity about the size of a walnut completely filled with blood-clot. Liver and spleen contained tuberculous nodules. Tubercles were also found in the kidneys, basal meninges and gray matter of the cerebral cortex.

E. Sluka⁵² believes that the diagnosis of apical tuberculosis in children is often a mistaken one. It is based on a picture resembling that of apical tuberculosis in adults, the presence of the tuberculous habitus, and of a pulmonary catarrh. Roentgen-ray pictures are a great help in clearing up the difficulty. They show apical tuberculosis to be exceedingly rare in childhood and the clinical picture to be the results of a thoracic deformity, either scoliosis or a cervical rib.

C. McNeil⁵³ believes that scrofula is more than a variety of tuberculosis and that it is the tuberculous infection in children who have lymphatic constitution. In an industrial school near Edinburgh, McNeil has had children with clinical manifestations of scrofula, who gave intense tuberculin reactions and in whom post mortem was discovered evidence of lymphatic constitution. Scrofula, due to a pyogenic infection in children with a lymphatic diathesis, however, is not unknown and has been described by Cornet.

Just what the lymphatic constitution is, is not clear, but McNeil thinks that the thyroid gland is involved in this condition.

Hutinel⁵⁶ reports a case of tuberculous pericarditis in a 13-year-old boy. The child was brought to the hospital for a fever of eight days' standing. On entrance the most prominent symptoms were marked dyspnea, slight cyanosis, and a temperature ranging between 39 and 40 C. Examination showed numerous râles over both lungs, an area of diminished resonance at the left apex with a rough inspiration and expiration and a few subcrepitant râles. The heart-sounds were diminished and the pulse rapid and small. A few days later signs of fluid appeared at the left base and 250 gm. of pus were removed by puncture. The heart-sounds became more dull and distant; dyspnea and cyanosis were intense. A pericardial puncture was made, but no fluid obtained. A second puncture yielded 40 gm. of bloody fluid. The temperature fell and the dyspnea was relieved after puncture. The cyanosis persisted and the liver enlarged until it occupied nearly the entire abdomen. A diagnosis of tuberculous pericarditis was made.

Hutinel describes three forms of tuberculous pericarditis: (*a*) the latent form; (*b*) the fibrinous form; (*c*) pericarditis with effusion. The latent form is not very rare and is often discovered at necropsy. In this form miliary tubercles, either discrete or conglomerate, are scattered over the pericardium. Fibrinous pericarditis is only exceptionally of tuberculous origin. The pericardium is obliterated and the tubercles are found beneath the fibrinous plaques. Hutinel's case illustrates the third form.

A. L. Goodman⁵⁹ reports a case of tuberculosis of the testicle in a 2-year-old child. The swelling had been apparent for a few months and had steadily increased. There was no pain or tenderness. The

patient was operated on and a tuberculous epididymitis found. Goodman says that tuberculosis of the testicle in children is either a primary isolated manifestation or a secondary complication of a visceral tuberculosis. Primary tuberculosis is usually unilateral and does not extend above the inguinal ring. Usually the tuberculous mass remains encysted, but sometimes it suppurates and causes fistulas. Secondary tuberculosis of the testicle is more extensive. Clinically, the symptoms may be acute or chronic, and the second condition is revealed accidentally or by the appearance of abscess or fistula.

The prognosis of the primary forms is good, but that of the secondary unfavorable.

F. C. Pybus⁶⁰ reports the following case of tuberculosis of the tunica vaginalis in a 3-year-old child. According to the history, a swelling had been noted in the left side of the scrotum soon after birth. The only abnormality found by Pybus was a swelling in the left scrotum, which was evidently of the testicle, globular in shape, hard and non-translucent. It was impossible to distinguish testicle from epididymis. The cord was slightly thickened. A diagnosis of tuberculosis of the testicle was made and operation advised. At the operation an incision was made on the anterior surface of the swelling. After going through new tissue a quarter of an inch thick, the tunica vaginalis was opened. As it was impossible to dissect off the thickened tunica vaginalis, castration was performed. The specimen showed a remarkable swelling of the tunica vaginalis, whose inner surface was slightly granular. Testicle and epididymis appeared normal. Microscopic examination of the tunica vaginalis showed that it consisted of hyperplastic tuberculous tissue containing many giant cells. Pybus thinks that infection took place from the abdominal cavity, although there was no evidence of abdominal tuberculosis.

S. Boyde⁶¹ reports a case of tuberculosis of the kidney in a 3-year-old child, who was admitted to the hospital because of bronchopneumonia and pyuria. The left kidney gradually increased in size and tubercle bacilli were isolated from the urine. The cystoscope showed the orifice of the left ureter to be reddened and ulcerated. The child was operated on. She recovered from the operation, but died six months later from phthisis. At necropsy the right kidney was found normal, an unusual occurrence, as in most instances tuberculosis of the kidney in children affects both organs.

A. Fischer⁶² reports a case of tuberculous duodenal stenosis in a 10-year-old child. Clinically, the picture was one of pyloric stenosis. The child was operated on, and it was found that the stenosis was caused by a circular scar, 2.5 cm. wide, located 1 cm. below the pylorus within the duodenum. The diagnosis of tuberculosis was based on the

circular character of the scar and the presence of other tuberculous lesions. Gastro-enterostomy was performed and the child recovered.

A. Tietze⁶³ reports two instances of tuberculosis of the liver in boys of 5 years. Marked enlargement of the liver and spleen developed in the course of a pulmonary tuberculosis which had lasted for months. There was no fever or tenderness, but a large amount of ascites. Lues and alcoholism were excluded; the von Pirquet tests were positive. Talma's operation was performed, and in one case a small piece of the liver excised. This showed undoubted tuberculous changes. The operation had no effect on the course of the disease.

F. W. Schlutz⁶⁴ has studied the subject of absorption of fat from the intestinal tract of the actively tuberculous child. He thinks the subject important, because it is an almost universal custom to give the tuberculous child a diet especially rich in fat.

Schlutz first calls attention to Weigert's experiments, which proved that the tissues of animals fed on protein and fat-rich food showed the largest amount of fat-free residual substance and were low in water content, while, conversely, those fed on food low in protein and fat, but rich in carbohydrates, showed a small percentage of fat-free residual content, but retained much fluid. Weigert has further demonstrated that animals fed on carbohydrates and with pronounced water retention in their tissues are the least resistant to tuberculous infections, while those fed on fat-rich mixtures, resulting in low water retention, succumbed much less readily to the inroads of this disease.

Schlutz' series of twenty cases comprised all the common forms of tuberculosis. An exclusively fat-rich diet, consisting of milk, cream, butter and eggs, with a small addition of carbohydrate, was given in fifteen cases and the same diet with a larger addition of carbohydrate in five cases. The fat absorption was distinctly diminished only in the glandular type of tuberculosis. In all other forms it very nearly approached the normal. The additional amount of carbohydrate as given in the five cases seemed to improve the fat absorption. From these experiments Schlutz concludes that if it were a question of fat absorption only, high fat feeding would not be contra-indicated in most forms of tuberculosis. He says that experimental and clinical evidence both seem to show that a diet which insures the largest amount of fat deposit in the tissues with the least retention of water is the one most beneficial to the tuberculous child.

B. Marfan⁶⁵ discusses the subject of tuberculous peritonitis in infancy. Below the age of 2 years, he says, the disease is rare, the clinical picture is not clear and diagnosis remains obscure for a long time — often, in fact, until some acute tuberculous process, like bronchopneumonia, reveals it; or the child dies and the tuberculous peri-

tonitis is found at necropsy. Intermittent abdominal pain, slight digestive disorders, constipation alternating with diarrhea may be the only symptoms, or marked abdominal distention may be the only symptom. The temperature is usually subnormal, although occasionally there is an irregular intermittent fever.

Tuberculous peritonitis among infants is more grave than among older children and is always fatal among infants below 1 year of age.

Marfan reports a case of tuberculous peritonitis in a 14-month-old baby, and, from the study of this case and others, concludes that chronic tympanites without diarrhea or constipation in very young children usually indicates a tuberculous peritonitis or tuberculous mesenteric glands without involvement of the intestine.

E. Bruusgaard⁶⁷ discusses acute disseminated tuberculosis of the skin in children. He says that in most instances the acute lesions which develop at the close of acute infectious diseases in children are of tuberculous nature. The forms which occur are the disseminated miliary lupus, *gommies scrofulceuses*, lichen scrofulosorum, the hemorrhagic miliary tuberculid and various combinations of these lesions.

Bruusgaard reports a case of tuberculosis of the skin following an attack of measles in a 4-year-old girl. When examined six months after the measles, she had on the forearms, in the gluteal regions and on the lower extremities millet-seed to pea-sized nodules, extending into the subcutaneous tissue, and above the surface of the skin, which was red or bluish red in color. Some of the lesions fluctuated, others had broken on to the surface of the skin and gave a typical picture of *gommies scrofulceuses*. Besides these multiple subcutaneous lesions were many small, round or oval verrucose papillary lesions. Guinea-pigs inoculated with the puriform content of the nodular and with excised portions of the papular lesions died of tuberculosis. The child died of tuberculous meningitis.

M. Bourgeois⁶⁸ says that lately the subject of metastatic hematogenous tuberculosis of the skin has received considerable attention in medical literature, and lesions not having the classical structure of tubercle are now regarded as tuberculous.

Bourgeois reports two cases of metastatic hematogenous tuberculosis of the skin in children of 7 and 3 years, neither of whom had previously shown any evidence of tuberculosis. Shortly after measles in one instance and scarlet fever in the other there developed rapidly and simultaneously in several locations on the skin lesions partly characteristic of lichen scrofulosorum and partly of the papulonecrotic tuberculid, but to the greater extent characteristic of tuberculosis verrucosa cutis. The lesions consisted of hard verrucose papules, unequal in size and irregularly grouped. They were covered by a thick

adherent horny layer with a livid red sharply defined edge; were principally on the extremities (hands and feet), but also on the elbows and knees, buttocks and face. They appeared in crops, ran a chronic course and gradually more and more resembled a verrucose lupus vulgaris.

From a study of these two cases and others reported in the literature, Bourgeois comes to the conclusion that besides the usual form of tuberculosis verrucosa cutis due to exogenous infection, there exists a second disseminated hematogenous form. This form usually occurs in children after an acute infectious disease. Associated with the lesions typical of tuberculosis verrucosa cutis are those of other hematogenous tuberculids as the papulonecrotic tuberculid and lichen scrofulosorum. The clinical picture is that of the exogenous form.

S. T. Champtaloup⁶⁹ reports an unusual case of multiple subcutaneous tuberculosis following circumcision. The baby was circumcised when 7 weeks old. The wound suppurated and three weeks later abscesses formed in the groins. One week later a measles-like eruption developed on the face, body and limbs. This all faded except several small areas, which indurated and suppurated. As each indurated area softened it was incised, but failed to heal after several months' treatment. Champtaloup saw the patient eight months after the circumcision. The child was emaciated and hectic. There were numerous subcutaneous suppurating foci. On the outer margin and sole of the right foot and on the left instep were several discharging sinuses. On the inner surface of the right upper arm were recently healed scars surrounded by indurated tissue of a purplish color. On each buttock and on the right cheek and over the right lower jaw were superficial ulcerations. In the right inguinal region a small abscess was pointing. This was aspirated and the pus inoculated into two guinea-pigs. Both showed well-marked tuberculosis when examined four weeks later. Smears and cultures from the aspirated pus failed to show the tubercle bacilli.

The child was treated with tuberculin and eight months later all lesions were healed.

Champtaloup learned that the physician who operated on the baby was suffering at the time from a tuberculous laryngitis; hence the infection.

J. von Bokay⁷⁰ has collected reports of thirty-four cases of healed tuberculous meningitis from medical literature and reports three of his own. In twenty-nine of the thirty-four cases the diagnosis was substantiated by finding the tubercle bacilli in the lumbar fluid either by direct examination or by inoculation into animals.

Von Bokay's three cases follow: The first patient was a 12-year-old boy who developed the symptoms of a diffuse meningitis directly after an attack of measles. Lumbar puncture gave 45 cm. of clear fluid, which was evidently under pressure. After a few hours a coagulum formed. Microscopic examination showed only a few lymphocytes. The symptoms remained unchanged and lumbar puncture was again performed. The fluid this time contained many lymphocytes and a few tubercle bacilli. Two days later improvement set in and continued. Lumbar puncture was performed in all four times. The fluid injected into guinea-pigs caused tuberculous lesions. At the time of this report, two and one-half years after the disease, the child is in good condition, there is no sign of paralysis, and mental development is progressing favorably.

The second patient was an 11-year-old boy whom von Bokay was treating for tuberculous peritonitis. On the twelfth day after admittance to the hospital the boy became somnolent and complained of headache. Lumbar puncture gave 25 c.c. of clear fluid under high pressure. Meningitis was suspected and seemed probable because of arrhythmia of the pulse and positive Trousseau and Kernig signs. The symptoms did not subside, so lumbar puncture was repeated, in all, eight times. After the seventh puncture, improvement set in and continued, and the child was discharged from the hospital six weeks after admittance. The lumbar fluid was inoculated into two guinea-pigs, and in this case also gave rise to tuberculous lesions.

The third patient was a 7-year-old boy who entered the hospital with symptoms of meningitis. Lumbar puncture gave 20 cm. of clear fluid, which contained many lymphocytes, but no tubercle bacilli. There was no change in the child's condition and lumbar puncture was repeated. This time tubercle bacilli were found in the fluid. The child was taken home by his parents and so improved as to be able to get out of bed. Five weeks later he died. He was examined just before death by von Bokay, who found an advanced lesion of the left lung.

No recovery occurred in children under 2 years of age; the proportion of recoveries increased after 5 years, although only 10 per cent. of the cases of tuberculous meningitis occur in children over 7. The recoveries occurred, in general, when the tuberculous process was limited to the meninges or did not to any extent involve other organs.

As regards the lesions, von Bokay thinks they can be healed, even when specific changes, as congestion, hemorrhage and formation of miliary tubercles, have taken place. He quotes Ziehen, who says that in tuberculous meningitis in children wide-spread tubercle formation is absent, and there occur collections of only epithelial cells and

lymphocytes, but no giant cells. Also from anatomic-pathologic experience it is to be noted that a tuberculous serofibrinous meningitis without the formation of tubercles occurs, and it is these forms that are more likely to heal, as also those in which the tubercle bacillus causes only a simple hyperemia.

The only method of treatment to consider is operative. Von Bokay mentions reports by several writers of cure by trephining the skull and draining the subarachnoid space. He thinks that this method is indicated in some cases. In cases in which the pathologic changes are such as will allow of cure, systematic lumbar puncture is indicated, but von Bokay thinks that an important factor is the natural resistance of the organism to the tuberculous infection.

Barbier⁷¹ reports the instance of a child of 8 years who had had several transitory attacks of meningitis. Nov. 20, 1912, he was admitted to the hospital with a pleural effusion. He coughed, and tubercle bacilli were found in the sputum. He gradually improved except for a slight exacerbation in December, but in March, 1913, meningeal symptoms developed. Improvement again set in, but in April there was an exaggeration of the meningeal symptoms. Headache, vomiting and somnolence appeared; there were exaggerated reflexes, irregular pupils and pulse, and tubercle bacilli were again found in the sputum. These gradually disappeared, but new areas of involvement were found in the lungs. In May and June there were again attacks of vomiting and headache.

The child was last examined Jan. 24, 1914, and showed signs of congestion at the right apex, and a small new area in the left axilla. He had increased reflexes — all that remained of the meningeal attacks.

P. A. Potter and E. W. Blakely⁷² report the recovery from tuberculous meningitis of a 3-year-old boy who had entered the hospital, April 16, 1913, with the clinical symptoms of a meningitis. Lumbar puncture was performed and a clear fluid which was found to contain tubercle bacilli was withdrawn. Improvement followed the puncture. On April 20 lumbar puncture was again performed and 25 c.c. of rather cloudy fluid obtained. Relief of pressure seemed again to cause amelioration of the child's condition. During the following two weeks the fluid was removed eight times, and at the end of this time the signs of the disease were unmistakably less. Improvement continued; June 12 the lumbar fluid showed no tubercle bacilli and the child was discharged from the hospital, cured.

H. Finkelstein⁷⁴ says that lately recovery from tuberculous meningitis has rather frequently been reported, but that some cannot be proved not to be cases of serous meningitis, for the diagnosis was not substantiated by finding the tubercle bacilli in the lumbar fluid or by

animal experimentation. Even if tubercle bacilli were found, it cannot be proved that there was not a circumscribed tuberculosis of the meninges and not a true tuberculous meningitis, that is, a miliary tuberculosis of the pia mater.

Finkelstein reports a case in which necropsy proved the process to be a serous meningitis, resulting from the irritation of a localized tubercle. The patient was an 8-months-old boy with a spina ventosa of two fingers. For five weeks after admittance to the hospital he improved. Then he developed a pneumonia which had its crisis on the sixteenth day. Just before the crisis symptoms suggesting meningitis appeared. The child was restless and vomited occasionally; he put his hand to his head, as if in pain. There was stiffness of the neck, strabismus, facial paresis, irregular pulse. Then the child became soporous and the fontanelle was tense and bulging. The possibility of the process being a serous meningitis complicating a pneumonia was disregarded on obtaining under pressure 360 mg. clear fluid containing many lymphocytes, not polymorphonuclear cells, as occur in pneumonia. The further course of the disease proved the pulmonary lesion to be tuberculosis. After remaining normal for two days the temperature rose again. The signs of pneumonia did not clear up, the bronchial breathing became amphoric. The signs of meningitis, however, gradually disappeared so that none existed by the nineteenth day. The child died of a caseous pneumonia the thirteenth week of illness.

Necropsy showed no tuberculosis of the pia. The left ventricle was slightly distended; the ependyma was unchanged except for a thickened area over the caudate nucleus. A cross-section of the area revealed a pea-sized, caseated tubercle. Finkelstein offers the following explanation of the symptoms: During the course of a febrile tuberculous process in the lungs a few tubercle bacilli were liberated and localized in the brain beneath the floor of the left lateral ventricle. These bacilli caused a local inflammatory reaction and a serous meningitis of the ventricles. Encapsulation of the tubercle and subsidence of the meningitis caused the symptoms to disappear.

In a former report, D'Espine⁷⁵ called attention in cases of tuberculous meningitis to disturbances in equilibrium due to localization of the lesions in the superior vermiciform process. He now reports a case in which the early appearance of the ataxia made the diagnosis of tuberculous meningitis possible.

The patient was a 2½-year-old boy. He came under D'Espine's observation with the diagnosis of acute gastritis. For two weeks he had had attacks of vomiting, headache and slight fever. On examination the tongue was found coated, the pulse slow (60-68), with slight arrhythmia. There was no Kernig's sign and the eyes were normal.

When the child stood up, there was an ataxia with a tendency to fall backward. The diagnosis of tuberculous meningitis was based on this symptom. The diagnosis was corroborated the next day, when strabismus and Kernig's sign developed. Lumbar puncture gave a clear fluid with an increase in lymphocytes. The symptoms of cerebral pressure became more marked and the child died. At necropsy, besides the usual findings of tuberculous meningitis, a greenish gelatinous exudate was found covering the anterior half of the superior vermiciform process, and on the posterior half was a tuberculous nodule, about the size of a pea, which extended a little more to the left than the right. The lungs showed a miliary tuberculosis, with a large yellow caseating nodule in the base of the right lung.

P. S. Chancellor⁷⁶ reports hemiparesis and hemiplegia as early symptoms in a case of tuberculous meningitis. His patient was a 3-year-old girl, whose mother had died of tuberculosis. Five days before admission to the hospital the child was constipated, complained of feeling tired, and the next day vomited. Two days before admission attacks of convulsions occurred. Twitching of the left eye and of the left side of the body was noted during the attacks. The following day the left arm and left leg were partially paralyzed. There was no rigidity. On admission, March 22, the child was drowsy and did not move left arm or left leg. A Babinski reflex was present on the left side. The von Pirquet reaction was positive and tuberculids developed on the fourth day after admittance. The lumbar fluid was clear and escaped under some pressure. There was a choked disk noted on the thirteenth day. Meningeal symptoms became more marked and the child died on the seventeenth day.

This case, according to Chancellor, belongs to the type of tuberculous meningitis characterized by an early onset of more or less pronounced paralysis limited to one side of the body, rapidly developing into a general paralysis.

TUBERCULOSIS OF THE TRACHEOBRONCHIAL GLANDS

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Warnecke⁷⁷ discusses the symptoms which he considers of greatest value for diagnosis of bronchial gland tuberculosis. The presence of the combination of symptoms regarded as "lymphatic diathesis" are of importance. In adults as well as children are observed the pasty look, the swollen lips, thick nose, rhagades, swelling of the lymphatic tissues, inflammations of cornea, phlyctenular conjunctivitis, and catarrh of the upper air-passages. An important symptom is the brassy cough which becomes more pronounced after injection of tuberculin.

Among the objective symptoms which Warnecke deems significant are changes in percussion note over the sternum at the level of the second and third rib, as well as a change in the note in the interscapular space and over the spinous processes.

Auscultatory findings are confirmatory. Characteristic is an expiratory note, almost like a muscular sound, which is heard in the interscapular region and which is more marked after an injection of tuberculin. D'Espine's sign serves good purpose in children, but not in adults.

The blood examination is valuable. In active tuberculosis of the thoracic glands there is a relative lymphocytosis which can be increased by injection of tuberculin.

As regards Roentgen-ray findings, there is no doubt that Roentgen-ray plates show enlarged glands as well as inflammatory infiltrations, peribronchial and perilymphatic processes at the hilum and interlobular exudates. Shadows of interlobular exudate indicate the presence of a Ghon's primary lesion, as this is always accompanied by a pleurisy.

W. Götz⁸⁹ discusses the value of the various symptoms of enlarged bronchial glands after following and examining the history of sixty-eight patients. Frequently in instances of enlarged bronchial glands a history of hereditary or family tuberculous taint is obtained, although this can never be sufficient reason for making the diagnosis. First must be considered the symptoms. Failure to develop, pallor, loss of weight and cough are suspicious. There is no characteristic type of

fever. Many of Götz' patients were free from fever; a number had a slight rise; a few had at times a marked elevation, a few long febrile periods, due to the action of the tuberculo-toxins. Evidence of scrofula is frequent, Götz finding it in forty-three of his patients. Symptoms due to direct pressure on the nerves are less frequent than those due to pressure on the veins.

As to physical findings, Götz believes the difference in the percussion note over the apices to be of great value. This is not due to pulmonary involvement, as is shown by the Roentgen ray, but to changes resulting from pressure of the enlarged glands. The most important area of dulness due directly to the enlarged glands is found over and to both sides of the sternum. Dulness over the vertebra is less important, but Götz found it over the third and fourth vertebra in fifty-three of sixty-five cases and that is lower than occurs normally.

The most valuable of the auscultatory signs is that of d'Espine, namely, bronchophony over the spinous processes at a lower level than normal—the seventh cervical vertebra in small children, the first thoracic in children of 8 years, and the second in children of 12 years.

Götz was surprised to see how seldom the Roentgen-ray pictures conformed with the clinical findings. There occurred, however, in most of his cases on both sides of the median shadow and especially on the right side, streaks and round shadows which were not found in pictures of normal chests and were undoubtedly enlarged bronchial glands.

Of value in diagnosis is a marked diazo reaction, if other causes of the reaction can be ruled out.

C. Riviere⁵¹ discusses the diagnosis of enlarged bronchial glands and phthisis. He lays particular stress in the diagnosis of enlarged bronchial glands on the finding of dulness by percussion in the right interscapular region. He says he was the first to call attention to this finding and thinks it due to pressure on the right pulmonary artery, as it passes in front of the bifurcation glands. Normally, there exists on each side of the spine, between the first and fifth dorsal vertebra, extending one inch from the middle line, an area of slightly impaired resonance elicited by gentle percussion. In enlarged bronchial glands the impairment on the right side becomes more marked and extends out 2 or 3 inches from the middle line and downward to the sixth, seventh or even eighth vertebral spine. Almost always there is also an impairment of resonance over the apices, and this often leads to an erroneous diagnosis of phthisis.

The diagnosis of phthisis in children is but little removed from the diagnosis in adults. The most valuable of all physical signs are those obtained by gentle percussion.

S. Maggiore⁸² examined with the Roentgen ray 131 children with enlarged thoracic veins. In but twenty-four cases was this the only symptom besides the enlarged glands in the Roentgen-ray plates. In most cases the size of the glands corresponded to the degree of venous enlargement. Maggiore believes that enlarged veins are pathognomonic of enlarged bronchial glands only when they are limited to the upper part of the chest. In most cases he found them in the second intercostal space, between the border of the sternum and the inner half of the clavicle. Less often they were in the first and third intercostal spaces. He found them more frequently on the right than on the left side or bilateral. He is of the opinion that enlarged thoracic veins are a valuable sign in the diagnosis of enlarged tracheobronchial glands.

E. Rist⁵⁵ agrees with Kusz, Albrecht and Ghon that enlargement and caseation of the bronchial and mediastinal glands are caused by and follow an initial pulmonary lesion. In tuberculosis in children caseous degeneration of glands is commonly observed. It may affect only a part of the gland, but in the greater number of cases, when tuberculosis is the cause of death, the whole of the enlarged gland is caseated. The caseous mass is surrounded by fibrous tissue, which adheres firmly to neighboring organs, as esophagus, trachea, bronchi, blood-vessels, and especially to neighboring lymph-glands. Compared to the findings in tuberculosis in adults the difference is very striking. In adults, extensive ulceration of the lungs is found post mortem in cases of long-standing tuberculosis, and the bronchial glands are of normal size or hardly enlarged. Instead of being fixed to the surrounding tissues by fibrous adhesions, they are easily enucleated, and — most important — they are rarely caseated. Rist quotes Koehler, who explains the difference by the fact that in adults the lymphatic channels become obliterated by chronic inflammation and scar tissue. Another explanation is that, in children who recover, the glands are changed into fibrous-anthracotic nodules, incapable of reacting to further tuberculous changes in the lungs. The difficulty in accepting this explanation is that the glands are not found post mortem to be anthracotic.

Rist thinks that the fact that the glands do not react in adults is simply another explanation of allergy of von Pirquet. They would react to any other inflammatory process but tuberculosis, which goes to show that tuberculosis in the adult is not a primary infection.

M. Paunz⁵⁶ article on rupture of tuberculous tracheobronchial glands is abstracted at length, not only because it is a valuable contribution to the subject of tuberculous tracheobronchial glands, but because the results obtained by Paunz' methods of treatment are important.

The tracheobronchial lymph-glands is the most frequent localization of tuberculosis in childhood. Even if tuberculosis of these glands cannot be diagnosed clinically, it is the usual accompaniment of pulmonary tuberculosis, miliary tuberculosis, tuberculous meningitis, osseous tuberculosis and intestinal tuberculosis. Necropsy findings have shown that tuberculosis of the tracheobronchial glands is almost always a secondary infection, that is, the result of a primary infection in the lungs. According to Küssz, inhalation tuberculosis causes an especial form of tuberculosis in children, which clinically cannot be diagnosed, but can be revealed by careful examination at necropsy. The form is characterized by a small nodule, sharply defined from the surrounding pulmonary parenchyma and situated beneath the pleura. Here it remains in this condition for years, or it may soften and empty its contents into a bronchus. The regional lymph-glands show constant tuberculous changes, but the lymph-passages between the primary pulmonary lesion and the regional lymph-glands remain unaffected. It is possible, however, according to Küssz, that the tubercle bacilli, which reach the finest bronchioles, can be taken up into the lymphatics and deposited in the glands without producing a primary lesion in the lungs.

In his article Paunz defines as tracheobronchial glands those located in the angles of division of trachea, the bronchi and collateral branches of the bronchi, besides the chains of glands surrounding trachea and bronchi. The position of these glands presupposes that pathologic changes in them are accompanied by changes in the trachea and bronchi—the two most important being compression of and rupture into them. As regards the pathology of tuberculous tracheobronchial glands, it has been proved by inoculation experiments that the glands can contain bacilli without any tuberculous lesions. Usually, however, shortly after infection they contain small tubercles, which later become confluent, caseate and soften, so that the whole gland consists of a softened mass surrounded by a thickened capsule. The gland may not be entirely softened, but may contain smaller or larger glandular sequestrae. These changes are accompanied by a periadenitis which causes pressure on the walls of the trachea and bronchi. Rupture into the air-passages usually begins slowly and with a small perforation, hardly as large as a pin-head, often with multiple sieve-like openings, or suddenly, with a large opening. The immediate effect of rupture is obstruction of the trachea and bronchi, which, if the sequestrae are large enough, will lead to suffocation. In gradual perforation the small softened masses are aspirated into the finest bronchioles and cause a caseous bronchopneumonia. The gland may at the same time perforate a large blood-vessel and cause death from suffocation and

loss of blood. The pericardium, esophagus, or pleura can also be broken into.

Tuberculous tracheobronchial glands in children can heal. Then there is absorption of the caseated masses, with calcification and encapsulation. Later, following whooping-cough or measles, the apparently inactive lesion can awaken and give rise to tuberculous bronchopneumonia, meningitis, or to a miliary tuberculosis.

In older reports the diagnosis of rupture of tuberculous tracheobronchial glands was made only post mortem. Lately, in medical literature appear reports in which the diagnosis was made before death. In these cases, for the most part, a foreign body was suspected, and the diagnosis of tuberculous lymph-gland made only after the gland was removed, or coughed up after a tracheotomy. Spontaneous cure of rupture occurs, as is evidenced by the finding of old scars post mortem.

Clinically, the manifestations of ruptured glands are overlooked or recognized too late, but direct tracheobronchoscopy offers, according to Paunz, great aid in making the diagnosis. He adds to a previous report of four cases of ruptured tracheobronchial glands, four more in which the diagnosis was made by tracheobronchoscopy. His first case was that of an 8-year-old child who was brought to the hospital with great dyspnea and hoarse voice. She had after entrance repeated suffocative attacks and there was a weakened respiratory murmur on the right side. A foreign body in the respiratory passages or ruptured tuberculous glands was suspected. Tracheobronchoscopy was performed with the patient in the upright position. Two cm. above the bifurcation soft flocculent masses floated before the field of vision, and when the patient lay down these were partly coughed out through the tube and partly removed by forceps. After the debris was sponged out, the right wall of the trachea above the bifurcation bulged markedly, and on the outer and anterior wall of the principal bronchus the point of rupture could be seen. After the operation the symptoms of tracheobronchial stenosis disappeared and the child was dismissed cured.

The second case was that of a 4-year-old child brought to the hospital with a diagnosis of enlarged bronchial glands with compression. Roentgen-ray pictures substantiated the diagnosis. Symptoms of suffocation appeared suddenly and operation was decided on. Tracheobronchoscopy showed that the principal bronchus was obstructed 1 cm. above the bifurcation by a bulging mass covered by mucous membrane. Paunz seized this with forceps and brought out first a pea-sized, then a bean-sized piece of gland. After this the bulging partly disappeared and the tube was farther inserted. A caseated piece of gland was pushed into the tube and afterward was removed by forceps; there then could be seen on the inner-anterior wall a round perforation.

Bronchitis and caseous pneumonia followed the operation, but the child finally recovered.

The third case was that of a 20-month-old baby. Tracheobronchoscopy confirmed the diagnosis of compression of the trachea and bronchi by tuberculous glands. The point of compression could plainly be seen, but no point of perforation could be found, although the tube filled with caseous matter. The child died five days after entrance with symptoms of suffocation. Necropsy showed, besides tuberculosis of the tracheobronchial glands, a wide-spread miliary tuberculosis.

The fourth case was that of a child of 3 admitted to the hospital because a foreign body in the air passages was suspected. Bronchoscopy showed stenosis due to pressure of the bifurcation glands. Suffocation symptoms following bronchoscopy necessitated tracheotomy, and tracheobronchoscopy revealed a small mass in the bronchus leading to the right lower lobe. The mass was not removed and the symptoms slowly subsided.

The two chief symptoms, according to Paunz, on which the diagnosis of enlarged bronchial glands is made are cough and dyspnea. The cough is spasmodic and has a metallic sound, and is non-productive. The dyspnea is inspiratory as well as expiratory. In infants it is chiefly expiratory. A point of importance is that, in spite of the severe dyspnea, the voice is clear, which shows that the obstruction is not in the larynx, but in the lower air-passages. Weakened respiration limited to one side is an important sign. The picture changes, when rupture of the gland begins. If a large caseous gland ruptures suddenly, a severe suffocative attack occurs just as in cases of aspiration of a foreign body. Suffocative attacks occur also with the entrance of a small amount of caseous debris into the air-passages and, as there usually exists first a small opening, which gradually becomes larger, these suffocative attacks are often the first symptom of rupture. Usually, too, there intervenes between the first attack of suffocation and the final catastrophe a few days or at least hours, so time is given for surgical interference. In each of Paunz' cases a number of days intervened between the first suffocative attack and the one which threatened life.

The appearance of subcutaneous emphysema is another evidence of ruptured tuberculous glands.

Paunz also discusses other signs, which have been designated as signs of enlarged tracheobronchial glands: multilateral enlargement of veins in the neck, changes in percussion note over manubrium and vertebrae, the Roentgen-ray findings; but as most important he regards direct tracheobronchoscopy. He says that to be of any value this must be performed under deep narcosis. Bulging of the wall can then be

made out, and this occurs more regularly on the lower part of the right lateral tracheal wall and the "mediale" wall of the right principal bronchus. The positions correspond to the locations where the tracheobronchial glands are found in large numbers. Direct tracheobronchoscopy also reveals a granulating or fresh point of perforation. It is evident then that tracheobronchoscopy is not only a valuable diagnostic aid, but is a means of determining the exact point of compression and rupture and allows of watching the development of the case.

As to therapy of these condition, therapy of rupture or beginning rupture must be sharply separated from that of compression. There is no doubt that good results can be obtained in cases of slight compression by the general hygienic and dietetic measures recommended in tuberculosis. Severe grades of compression need hospital care, for the condition must be closely watched, as rupture can be expected at any time.

In case of rupture, tracheotomy followed by bronchoscopy is indicated. Tracheotomy alone helps in many cases, as it facilitates expectoration of the pieces of gland. Tracheotomy must always be performed before attempt is made to remove the gland, otherwise the free sequestrae will cause suffocative attacks. With Paunz' cases, in all ten cases of ruptured tracheobronchial glands treated by tracheobronchoscopy have been reported; seven patients were cured. The three deaths occurred among Paunz' patients. One was a 6-months-old girl, one a 20-months-old boy, both with miliary tuberculosis; the third was a 4-year-old child with a foreign body besides the enlarged glands. From these results it is evident that direct tracheobronchoscopy is a method by which the suffocative attacks of glandular rupture can be warded off. The method, however, is limited to removal of the free glandular sequestrae and contents of the glandular abscess. Abscesses clearly showing through the mucous membrane could be incised, but this is not recommended, for it cannot be determined whether these are connected with a pulmonary abscess or with the esophagus, which, when opened, would result in hemorrhage or produce a communication between the air-passages and esophagus.

Recovery from tuberculosis of the tracheobronchial glands has been shown to take place. Necropsies on children dying from other causes have shown this, and usually in tuberculous abscesses rupture is often the last process before spontaneous healing. So Paunz believes it is the duty of physicians in all cases of rupture to perform tracheotomy at once and tracheobronchoscopy, and to try to prevent death by suffocation.

A. Ghon⁸⁸ reports a case of rupture of a tuberculous bronchial lymph-gland into the bronchus. A child a year and a half old was

brought to the hospital because of symptoms of stenosis. Intubation was performed, but the patient died the following day. Necropsy showed that a softened lymph-node on the anterior surface of the right hilum had ruptured into the main bronchus of the right upper lobe. In the tracheobronchial and bronchopulmonary glands were extensive tuberculous changes. There was also a tuberculous pleuritis on the right side and a confluent pneumonia with miliary tuberculosis of the right upper lobe as well as a lobular pneumonia of the left lower lobe and a recent tuberculous ulcer in the small intestine with enlargement of the regional mesenteric glands.

G. Caronia⁸⁹ reports a case in a 7-year-old boy of suffocation due to the rupture of a caseated lymph-gland into the trachea. Intubation was performed when the patient entered the hospital, but two hours later he coughed up to the tube. As a foreign body was thought to have entered the trachea, tracheotomy was performed, but the child died shortly afterward. Necropsy showed that a caseated gland had ruptured into the trachea and obstructed the bronchi.

According to Hutinel⁹⁰ various conditions influence the prognosis of tuberculosis of the mediastinal glands. Their gravity is not in proportion to their size. Often large masses of glands sclerose and heal, while small ones are the source of a rapidly fatal miliary tuberculosis or of tuberculous meningitis. Age is an important factor in prognosis, for the younger the child the more serious the case is. In infants the lesions show no tendency to heal; they spread rapidly and become disseminated, and at necropsy there is found the same pathologic picture as in rabbits and guinea-pigs which have been inoculated with tuberculosis. In children from 3 to 5 years the prognosis is less grave, but experience teaches that most children of this age who develop a meningitis or generalized tuberculosis have caseated areas in their mediastinal glands. Older children living in favorable hygienic surroundings usually recover, but often suffer relapse and are in danger of a generalized tuberculosis after acute infections or exaggerated fatigue.

The prognosis is influenced by the presence of pulmonary lesions. If one finds associated with the mediastinal adenopathy unmistakable lesions at the apex then the prognosis is frankly bad. Impaired resonance and modification of the respiratory sounds have been found at the apices, without tuberculous involvement of these areas, and are due to pressure of the enlarged glands on the bronchi, veins or pulmonary tissue.

In infants the appearance of subcrepitant râles at the hilum is disquieting. It usually indicates a diffusion of the process into the parenchyma of the lung.

The prognosis is always grave when pulmonary lesions develop in subjects who have very large mediastinal glands.

Slight elevations of temperature do not unfavorably influence the prognosis, but marked prolonged elevations are of serious import. Tachycardia with or without arrhythmia is always a bad prognostic sign.

Secondary infections play an important rôle in the prognosis of tuberculosis of the mediastinal glands. Necropsies of children who die of miliary tuberculosis following whooping-cough, measles or influenza frequently reveal in the mediastinum a gland which has softened the influence of the infective process or ruptured into a blood-vessel and given rise to the generalized tuberculous process.

Nutritional disorders, which diminish the resistance of the organism, also have an unfavorable influence on the prognosis.

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From the study of the register and death certificates of Stuttgart, W. Weinberg⁶¹ compiled the following statistics: (1) the mortality among tuberculous women in the first year after confinement was only 15 per cent. above that from tuberculosis in other women of the same age; (2) among 4,000 marriages of tuberculous persons the death-rate of husbands showed 100 per cent. higher than that of the general population of equal age; (3) the fecundity of tuberculous women was sub-normal; (4) the death-rate from tuberculosis was higher in families with a hereditary taint than in other families, but infection from the parents during the first year of life did not seem considerable; (5) among 16,000 children of tuberculous parents, observed from birth to the end of the twentieth year, the death-rate was 46.8 and 48.1 per cent., while that of the offspring of people who had died from other causes was 40.2 to 40.5 per cent. The death-rate of children who had lost both parents from tuberculosis was 52.4 per cent. The death-rate depended on the time which elapsed between the birth of the children and death of the parents. With children born twenty years before the death of the parents the death-rate was from 42.8 to 45.72 per cent.; with those born in the last year, 65.59 to 75.09 per cent.; of those born in the last four weeks of life, 16.7 per cent. were still-born, and 83.4 per cent. died before they were 20 years old. The death-rate of children of tuberculous parents was greater in the first and fourth decade of life.

In order to study the child reared in a tuberculous environment, M. Fishberg⁶² observed all the children of tuberculous applicants for relief to the United Hebrew Charities of New York City. He investigated social, economic and hygienic conditions of the family, examined all children under 15 years of age, and applied the cutaneous tuberculin test. The investigation was carried out in 217 families who were found living in conditions favorable to the dissemination of the disease. Of 274 consumptives found among these people, only 112 slept in a separate room and 136 slept in beds by themselves; the rest shared their rooms or beds or both with other persons.

Of 1,129 persons comprised in this group of families, 792 were under 15 years of age. Nearly all of these children were reared on breast-milk, only 5.5 per cent. having been brought up on artificial food. Some mothers suffering from active tuberculosis were found suckling their infants, who apparently thrived as well as others of their class; many, however, became infected with active tuberculosis.

The weight of the infants was fairly normal, but that of the children over 4 years of age was deplorably short.

The examination of hyperplastic conditions of the nose, throat and pharynx confirmed the opinion that these, as well as scrofula, have nothing to do with tuberculosis.

The results of the tuberculin test showed that the tuberculous milieu did not materially increase the number of tuberculous children, over 6 years of age, but that among the infants under 4 years of age the proportion infected was considerably higher than among children living in a better environment.

The mortality of children under 14 among these children was rather high. The opinion entertained by many authors that infants less than a year old, when infected by tuberculosis, do not survive the disease was only partly confirmed by this investigation, for Fishberg has seen among these children many who were undoubtedly infected during the first few months of life and who yet survived and even presented a healthy appearance. It appears, however, that the prognosis depends largely on the age at which infection takes place, and that the danger of fatality is in inverse ratio to the age at which the children are infected.

Massive infection, such as Fishberg found among these children, is the most potent factor in the propagation of tuberculosis. To be effective, prophylactic measures taken against the spread of tuberculosis must be directed to preventing contact with individuals suffering from the disease.

P. Nobécourt and G. Schreiber⁹⁷ emphasize the necessity of removing the child from tuberculous surroundings at birth. They say that the infant is not born tuberculous, that tuberculosis only exceptionally is hereditary, that it is nearly always contracted after birth and that the contagion is from the family. Nobécourt and Schreiber urge that the work founded by Grancher for the preservation of infants should be furthered by a society. This society should remove infants from their infected surroundings, place them in the country, and exercise constant surveillance over them. The nurses must be selected with great care and be under strict medical inspection. Better than private boarding places, these writers think, are crèches located in the country, mountains or at the seashore.

C. Riviere⁹⁹ says that infection with the tubercle bacillus is inevitable for those living in crowded communities; that a mild infection is protective against further disease or against acute fatal forms; that a primary infection is always dangerous, but that the younger the infant the more serious is the outlook. Since infection is inevitable, the question has to be considered whether infection with the dangerous

human organism and through the more susceptible respiratory channel should be risked or whether there should be substituted alimentary infection with the comparatively innocuous bovine tubercle bacillus. Massive dosage, such as may occur from a single cow or small infected herd, is to be carefully avoided. Dilution of organisms in a well-mixed milk-supply reduces the risk of a gross infection to a minimum, and the matter may be still further elaborated by feeding only small quantities of unboiled milk at first and postponing its administration until the more dangerous early months are passed. Riviere then contends that complete extermination of bovine tuberculosis is not to be wished for so long as the human tubercle bacillus is rife. The aim should be a clean milk-supply and adequate inspection of small byres, and of single cows; through these measures the danger of massive bovine infection may be eliminated and the use of raw milk be more safely and confidently recommended.

T. C. McCleave¹⁰⁰ emphasizes the fact that while all recognize that infection in a very large measure results from contact with infected people, it is now also well established that in a certain smaller proportion of cases the disease is derived from tuberculous cattle. As bovine bacilli practically always gain access to the human body through the ingestion of contaminated milk or milk products, methods of prophylaxis must be directed toward the eradication of the disease from dairy herds, but more especially measures must be devised to render milk from even tuberculous animals suitable for dietetic use. Certified milk is the only commercial milk which affords reasonable assurance of safety, and it should be obtained for little children whenever possible. Commercial pasteurization should be considered adequate only when carried out under conditions which assure a fresh and not excessively contaminated supply, heated to a requisite temperature of 60 C. for a period of twenty minutes, quickly cooled and kept iced, delivered early and consumed without delay, for such milk is likely to undergo rapid fermentative changes. Such conditions, according to McCleave, can be enforced only by a system of strict and energetic official control, and, as carried out at present, are often worse than useless. He is of the opinion that the only absolutely safe milk is that which is heated in the home of the consumer. Milk which is brought to just below the boiling-point in the family kitchen will never transmit bovine tuberculosis to the babies.

W. C. White¹⁰² draws attention to a number of points in prevention of tuberculosis in children, which interest both the tuberculosis worker and the pediatrician. First he deplors the practice of midwife or obstetrician of removing mucus from the mouth of the new-born by direct mouth-to-mouth aspiration. He cites the report of Reich, who

collected ten cases of tuberculous meningitis in the practice of a midwife who suffered from pulmonary tuberculosis and who practiced this method of resuscitation.

Second, he mentions the danger of infection from nurses and nurse-maids and emphasizes the importance of examination of all persons who are to be intrusted with the care of babies and children.

The third point is the prevention of illness from the use of milk. White thinks that this can be effected only by a carefully supervised, municipally controlled milk-supply.

Another point is forbidding tuberculous mothers to nurse their babies. The danger is not so much that the child will become tuberculous from the mother's milk as that the mother may cough over it.

The next point discussed is that of the value of tonsillectomy in the prevention of tuberculosis. White suggests that careful records of cases in which the tonsils are removed should in the future be kept to give information of the value of this procedure in the prevention of tuberculosis.

Finally, White calls attention to statistics compiled by Frederick Hoffman, which show that in the last ten years the mortality of children under 5 years has dropped, but not that of children between 5 and 15. The figures suggest necessity for work of pediatricians and tuberculosis organizations during this period along the lines of such activities as open-air schools, school lunches, better home conditions, child labor, better workshops. While tuberculosis organizations have taken part in these activities, they belong no more to them than to the various other groups of workers who are interested in child life and health.

Mary E. Lapham¹⁰⁶ maintains that medical inspection of schools will protect children from exposure to infection with the tubercle bacilli; will promote their resistance by all hygienic measures available and will put children below par into out-of-door schools, or even under a tuberculosis régime.

J. V. Van Pelt,¹⁰⁸ discussing open-air schools in their relation to pulmonary tuberculosis, says that from a theoretical point of view they have the following advantages: The rapid flow and change of air is far more beneficial than the ordinary or even the best forms of so-called ventilation. Sunlight and strongly diffused light act as disinfecting agents. Fresh air is Nature's tonic and the vitality of individual is fortified. It must not be forgotten that, when discomfort is felt from the cold, the cold becomes a menace which counteracts the value of the fresh air.

Another advantage of the open-air school is that the nourishment of the children is supervised.

M. M. Vinton¹¹¹ says that a fresh-air class of the open-window type can be organized in any ordinary schoolroom. The ordinary window-sashes must be displaced by sashes swinging on pivots, four sashes in each window, and the entering air directed toward the ceiling. There should be seats fixed on small platforms, which can be moved about the room and allow space for reclining chairs, an addition to the ordinary equipment of a schoolroom. There should be a gas stove for heating milk, and scales for weighing the children.

This is practically the arrangement of the fresh-air schoolrooms in New York with which Vinton is associated. The classes there are ungraded and limited to twenty-five pupils. At 10:30 a. m. a luncheon is served and, after the children return from home at 1 o'clock they don sleeping bags and rest for an hour in reclining chairs. At 2 p. m. another lunch of crackers and milk is served.

Vinton says that the fresh-air class has solved the question of how pretuberculous children may profitably enjoy the benefits of outdoor air and be prevented from acquiring a tuberculous lesion of the lungs.

M. Solis-Cohen¹¹² says sanatorium treatment is incomplete unless the patients are instructed and drilled in the life they should lead after their discharge. With class instruction the good results obtained would undoubtedly be more lasting and relapses less frequent.

At the Jewish Sanatorium at Eagleville, Pa., Solis-Cohen gives such instruction to the children. These talks deal with the nature of tuberculosis, the avenues of infection, the ways to avoid communicating the disease, and the hygienic measures necessary to regain and retain health.

TREATMENT

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E. Müller¹¹³ discusses the treatment of tuberculosis in childhood under the following heads: (1) medicinal treatment; (2) general dietetic and hygiene measures; (3) surgical measures.

Among the chemical remedies, Müller believes creosote valuable because of its antidiarrheal and appetite-producing properties.

Müller thinks that there is a tendency to overfeed tuberculous children. A rapid increase in weight after a diet rich in starch and sugar is injurious. Experiments seem to show that a tissue rich in water, such as is produced by feeding carbohydrates, favors the development of the tubercle bacillus. Fats, on the other hand, are useful. Müller does not give much milk because of the large amounts of salts it contains, but 200 to 500 c.c. of cream daily, also abundant butter.

Fresh air and sunshine are important in the treatment of tuberculosis. The efficacy of sunshine in the treatment of surgical tuberculosis has been demonstrated in the last few years. Müller believes, however, that the moderate heat of the sun as experienced in his climate (Berlin) is more effective than the intense heat of mountainous regions. He thinks that with fresh air and sunshine a cure of surgical tuberculosis in children can be effected without operative interference. Müller thinks that salt-water baths are especially useful in the treatment of scrofula. The salt is gradually increased in strength from 3 to 8 per cent., and given three times a week for six weeks. The salt must be boiled for two hours, then the salt-lake poured through cheese-cloth into the bath.

Müller also discusses the subject of prophylaxis of tuberculosis in children. Infection with the bovine bacillus is comparatively small, as milk in Germany is always boiled. Ninety per cent. of the children are infected from their tuberculous families. Sanatoriums which only care for early cases and leave behind the advanced ones do not fulfil their true object and further progress in prophylaxis will not be made until advanced cases are segregated.

H. Vogt¹¹⁴ directs attention to dietary treatment and the use of pneumothorax and of tuberculin in tuberculosis of children. He does not believe in excessive use of carbohydrates and fat, for carbohy-

drates increase the body weight, but do not increase resistance against the disease. Vogt uses a moderate amount of milk and vegetables, and meat twice a day. Fat is given in form of cod-liver oil. With this diet the children do not gain weight too rapidly, but their color improves and their muscles harden.

Vogt believes that artificial pneumothorax is effectual for young children, even when both lungs are involved, provided one is not too extensively diseased. He regards this measure as the most important and reliable at hand for severe cases. It is really applicable to infants, because the disease spreads too rapidly to other organs. Time, however, must tell whether cures obtained by this treatment are permanent.

Vogt is not in favor of the tuberculin treatment, agreeing with Czerny that the results obtained with its use are no greater than obtained without it.

E. Nobel¹¹⁵ reports a case of unilateral pulmonary tuberculosis in a 7-year-old girl who was treated with artificial pneumothorax. In the upper lobe was a tuberculous infiltration which could be demonstrated clinically and with the Roentgen rays. Artificial pneumothorax was produced and maintained for three months. After the lung was again inflated it was found to be normal.

K. Bähr¹¹⁶ warns against judging the results of therapeutic agents in tuberculosis. He cites five cases of scrofuloderma in children under a year old, in four of which the healing was spontaneous. Cure was complete and not followed by any other manifestation of tuberculosis. The fifth patient was treated with Rosenbach's tuberculin. These cases show that scrofuloderma in the first year of life is often a benign condition and that cure of such cases is no test for the value of any tuberculin.

A. Stommel¹¹⁷ treated 22 children with tuberculosis with Rosenbach's tuberculin. Eighteen suffered from pulmonary and bronchial gland tuberculosis and 4 from tubercular peritonitis. Of the 18 children with pulmonary and bronchial gland tuberculosis, 6 showed a decided, 4 a slight improvement, 5 showed no change or slight aggravation of symptoms, 3 showed a decided aggravation of symptoms, with 2 deaths. Three of the 4 children with peritonitis improved under treatment.

From the results, Stommel came to the conclusion that Rosenbach's tuberculin did not produce a particularly favorable effect. There was no opportunity to observe a complete cure, and the improvement observed could not be ascribed unconditionally to the tuberculin, as similar and even better results have been obtained when children have been taken away from their unfavorable surroundings and given plenty of fresh air, sunshine and good food. Moreover, in the two

cases which came to necropsy the lesions showed no tendency to heal. Stommel, therefore, though he does not regard the remedy as dangerous, thinks it is therapeutically inert.

During the last year C. Beck¹¹⁸ has treated 45 infants and children with Rosenbach's tuberculin. The youngest child was 2 months old, the oldest 13½ years. Seventeen of the children had glandular tuberculosis, 11 osseous caries, 6 pulmonary tuberculosis, 5 peritonitis, 4 meningitis and 2 generalized tuberculosis. Enlarged bronchial glands were demonstrated by the Roentgen rays in all. In the cases of meningitis there was a fall in temperature, the children became quieter and had no further convulsions. Cases of generalized tuberculosis were influenced by the treatment. Beck thinks early cases of bronchial gland tuberculosis are best fitted for the treatment, but advanced ones can be cured. He thinks that Rosenbach's tuberculin should invariably be given a trial in tuberculosis in children.

D. W. McMichael¹¹⁹ speaks highly of K. von Ruck's vaccine, with which he obtained convincing results in treating more than 200 children and adults. While it is not, he says, a completely certain agent, it does all that any of the known specific products do to check the disease.

Treplin¹²⁰ thinks that a sojourn at the seashore favorably affects any form of tuberculosis. There is an increase in appetite and a corresponding gain in weight. Scrofulous children are especially benefited, and often wonderful results are obtained for children with open pulmonary tuberculosis. Children with surgical tuberculosis are benefited if they are in a hospital under the care of a skilful surgeon. Treplin urges that children with surgical as well as pulmonary tuberculosis should not be kept long in city hospitals, but should be sent to the seashore as soon as possible.

Discussing the treatment of surgical tuberculosis, P. Redard¹²³ says that heliotherapy is not advantageous in all cases. It is dangerous without proper immobilization, especially for children difficult to control. For severe forms, the classical methods, chiefly rigorous immobilization with orthopedic apparatus, ought to be the basis of treatment. In mild forms it is often advantageous to combine heliotherapy and immobilization with simple orthopedic apparatus. By this combination not only is a favorable effect on the general health obtained, but also the local disease heals without deformity and with functional integrity.

W. E. Ladd¹²⁶ discusses the treatment of tuberculous cervical adenitis in children. He says that the methods which demand attention are the open air and hygienic treatment alone or combined with tuberculin and palliative surgery, and the Roentgen-ray treatment. He is rather disappointed in the results obtained by palliative surgery and

tuberculin. With the Roentgen ray he has had limited experience, but, in the instance of superficial broken-down glands, which are slow to heal, three or four exposures will sometimes cause them to heal. The Roentgen ray will also sometimes close a sinus and make possible a clean dissection of underlying glands.

Heliotherapy has apparently yielded many good results, but is available only for patients who have sufficient means to go to high altitudes.

Ladd is of the opinion that thorough extirpation of all infected glands with the primary focus yields by far the highest percentage of cures, and requires far less time than any other means. He thinks, moreover, that tuberculosis of the tonsils is more common in cases of tuberculosis of the cervical glands than has been surmised. To avoid unsightly scars, the operation should be performed early before the glands have broken down. Hygienic measures play an important part in the postoperative treatment.

O. H. Peterson¹²⁷ discusses the Roentgen-ray treatment of tuberculous lymph-glands. He divides tuberculous lymph-glands into three groups: (1) simple hyperemic glands; (2) caseated and suppurative glands; (3) ulcerated glands with fistula formation.

In the first group the Roentgen rays cause a gradual diminution in the size of the glands, and separation of masses so that the individual glands can be made out. After a long time they become quite small, but never disappear entirely.

In the second group the Roentgen rays hasten the softening process. When the gland is softened, nothing further can be accomplished without surgical interference. A small incision should be made and the pus evacuated and the Roentgen-ray treatment continued, only after the wound has healed. Sometimes repetition of the procedure is necessary.

The third form is difficult to treat because secondary infection is always present. Closure of the fistulas sometimes follows the use of the Roentgen rays.

Comparing the results obtained by Roentgen rays with those of radical surgical procedures, Peterson says that in the former cosmetic effects, which are very important, are better and that all the tissue can be affected, while with surgical measures there is always a chance of overlooking a small infected gland. On the other hand, Roentgen rays only encapsulate the bacilli and the infection may flare up again. The length of time necessary for the Roentgen treatment is also a draw-back.

G. Jefferson¹²⁸ says that the radical removal of cervical glands is not unfraught with danger. Two children, aged 7 years and 3 years, operated on by him, died of a fulminating streptococcal infection, one

twelve hours, the other twenty hours after the operation. The source of the infection was probably the walls of the sinus, and Jefferson advises that the sinus be swabbed with iodine for a few days before the operation and that at the time of operation the wound should be washed out with saline solution and that drainage be employed, preferably through a separate stab wound.

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THE SCHICK TOXIN REACTION FOR IMMUNITY IN DIPHThERIA *

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As is well known, immunity in diphtheria is generally incomplete and of short duration. Even an attack of this disease with consequent stimulation of the body cells with diphtheria toxin and the formation of homologous antitoxin and other antibodies does not confer for any considerable length of time that immunity which is so characteristic of scarlet fever, measles and small-pox. Passive immunization with antitoxin confers an immunity even more fleeting, because the immune serum constituents are quickly eliminated or destroyed. For this reason, Smith, Park, and more recently von Behring have suggested an active form of immunization in diphtheria by means of toxin-antitoxin mixtures, as the antitoxin prepared by our own body cells is more lasting. In order to estimate the degree of immunity following injections of these toxin-antitoxin (T-A) mixtures, it is necessary to determine the amount of antitoxin per cubic centimeter of serum in units or fractions of a unit. For this purpose Römer's intracutaneous technic with the guinea-pig has been used, but the method is rather too uncertain and complicated for the routine examination of large numbers of persons.

Schick¹ has proposed a very simple clinical test for this purpose; it is based on the observations of von Behring that as little as one-hundredth of a unit of antitoxin per cubic centimeter of our serum will protect a person against diphtheria. Schick has determined that when an amount of diphtheria toxin equal to one-fiftieth the *minimal lethal dose* (M. L. D.) for a guinea-pig weighing from 250 to 300 gm. is injected intracutaneously in the human skin, if one-thirtieth or more antitoxin per cubic centimeter of serum is present this dose of toxin is neutralized and no reaction follows; if less than this amount of antitoxin is present or none at all, the toxin injected remains unneutralized and produces a local inflammatory reaction of erythema and edematous

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* From the Laboratory of the Philadelphia Hospital for Contagious Diseases.
1. Schick: Munchen. med. Wehnschr., 1913, lx, 2608.

infiltration. This toxin test may be used for determining the response to active immunization by means of the T-A mixtures; it does not, however, serve the purpose of a quantitative estimation of antitoxin in the body fluids, but is simply a ready clinical index based on the observation that, when properly performed, a negative test may be regarded as indicating that a state of immunity more or less satisfactory exists, whereas a positive reaction indicates the absence of antitoxin and a state of susceptibility to diphtheria.

It has also found a very useful and practical application in testing persons for natural diphtheria antitoxin, especially those who have been exposed to the infection. The logical conclusion would be that only those who react positively are susceptible to diphtheria and require passive immunization by means of an injection of antitoxin.

In this country the Schick test has been used quite extensively by Park, Serota and Zingher,² who report favorably on its practical value. We have been interested in this test during the past year, having made 1,265 inoculations, and are likewise able to subscribe to the value of the test, especially for the purpose of detecting those persons susceptible to diphtheria, on the basis that their blood contains no natural antitoxin or too small an amount for adequate protection.

The objects of this study were as follows:

1. To apply the toxin skin test to a large number of apparently normal persons to determine susceptibility to diphtheria at different ages.
2. To determine quantitatively the antitoxin content of the blood-serum of persons reacting positively, slightly positively, doubtfully and negatively in order to study further the toxin test under conditions in which the quantity of antitoxin in the blood is known.
3. To study the degree and duration of immunity to diphtheria in normal persons following an injection of diphtheria antitoxin.
4. To study the degree and duration of immunity among persons suffering with scarlet fever and receiving an injection of diphtheria antitoxin.
5. To study the degree of immunity during and following an attack of diphtheria.
6. To study the practical value of the toxin skin test in determining which persons should be immunized with antitoxin when exposed to diphtheria.

TECHNIC OF THE SCHICK TEST

Preparation of the Toxin.—It is advisable to prepare the toxin for this test from a strong diphtheria toxin in order to reduce by high

2. Park, W. H., Serota, M. H., and Zingher, A.: Arch. Pediat., 1914, xxxi, 481; Active Immunization in Diphtheria and Treatment by Toxin-Antitoxin, Jour. Am. Med. Assn., Sept. 5, 1914, p. 859.

dilution the amount of protein constituents of the bouillon medium to a minimum. The *minimal lethal dose* (M. L. D.) of a toxin is first determined by injecting varying amounts of the diluted toxin subcutaneously in a series of guinea-pigs weighing between 250 and 300 gm. The least amount of toxin killing a pig at the end of four days is the minimal lethal dose. For the test Schick uses one-fiftieth this amount of toxin so diluted that it is contained in 0.1 c.c.; Park uses the same amount diluted in 0.2 c.c.

After trying both methods we have adopted one-fortieth this amount of toxin as our dose and dilute it with sterile normal salt solution containing 0.25 per cent. phenol in such manner that it is contained in 0.05 c.c. With this technic we have produced less trauma and have fewer doubtful reactions.

Only ripened toxins should be titrated and used because the toxin deteriorates rapidly under ordinary circumstances. We usually dilute the L + dose of toxin³ 1:100, determine the minimal lethal dose and from this make up the 1:40 dilution for the Schick test. It is necessary to retitrate and make up fresh dilutions for the Schick test every two or three weeks and the toxin should always be kept at a low temperature to retard deterioration as much as possible.

Method of Injection.—The injection is made intracutaneously by pinching up a fold of skin between the index-finger and thumb and inserting the needle into the epidermis. As the injection is made a whitish spot develops and a slight stinging pain is felt; if this raised anemic area is not seen the injection is probably too deep and unsatisfactory.

A very fine needle (No. 26) and a perfectly adjusted syringe are necessary. We have used with much satisfaction the Record and Fournier's tuberculin syringes. Platinum iridium needles are especially useful, as they are readily sterilized in a flame and are thus adapted for giving a large series of injections.

Injections are readily given in the skin of the arm near the insertion of the deltoid muscle after cleansing with alcohol and drying the skin.

The Reaction.—This appears in from twenty-four to forty-eight hours after injection and is characterized by an area of erythema with a brownish tinge measuring from 0.5 to 2 cm. in diameter and accompanied by slight edematous infiltration of the underlying tissues (see accompanying plate). In colored persons the erythema can usually be seen, although not always sufficiently well to measure, but the edema is readily palpable. The reaction usually reaches its height in

3. We wish to express our thanks to Dr. A. Parker Hitchens for much of the L + toxin used in this study.

from forty-eight to seventy-two hours and then begins to fade within a week or ten days, accompanied by some itchiness and usually followed by a brownish pigmented area of some days' or weeks' duration. A slight superficial scaling, due to the necrosing effect of the toxin on the superficial epithelial cells is generally noticed. In the majority of instances there is no general reaction.

Occasionally, the reaction is so slight that the observer is in doubt whether to regard it as purely traumatic or a weakly positive result. For this reason we make the total amount injected 0.05 c.c. in order to reduce trauma to a minimum. We have regarded any reaction measuring more than 3 to 5 mm. in diameter as positive; a very faint areola with no palpable infiltration about the needle hole was regarded as probably traumatic and negligible.

Park and his associates have observed in a small proportion of cases what they term pseudoreactions characterized by earlier development, more infiltration and less sharply circumscribed lesions disappearing in from twenty-four to forty-eight hours leaving a faintly pigmented spot which does not scale. These reactions are regarded as local anaphylactic reactions due to protein contained in the bouillon medium. We have regarded all reactions except those evidently traumatic as positive; the extent of the reaction is modified by the presence of varying amounts of natural antitoxin in the blood of the patient.

It is to be remembered that the true toxin reaction is purely irritant and inflammatory, and due to the direct action of the toxin on the local cells; it is not an anaphylactic reaction due to the action of a protein split product (proteotoxin) or anaphylatoxin.

Cutaneous Method.—We have also conducted this test by abrading the skin of the forearm in two places by means of a von Pirquet scarifier. A drop of toxin ($L +$ dose = 0.82 c.c.) was then applied to the lower of the two scarifications and gently rubbed into the tissues for a few seconds.

At the end of from twenty-four to forty-eight hours a small area of erythema could be readily seen about the inoculation site in most persons who showed a positive intracutaneous reaction. In colored children the edema could usually be appreciated by mere inspection or palpation.

We used the two methods of inoculation simultaneously in a large number of persons, but prefer the intracutaneous method, as by the cutaneous test the results are more difficult of interpretation and the inoculation more painful to the patient.

THE TOXIN REACTION IN PERSONS OF VARIOUS AGES

The toxin test was applied in 447 persons, most of whom were apparently healthy and well; a few were suffering with various chronic

diseases and were tested while undergoing observation and treatment in the wards of various hospitals in Philadelphia.

The results are summarized in Table 1.

The reaction has demonstrated that children between the ages of 1 and 8 years are most susceptible to diphtheria. It also shows that a small percentage of children under 1 year of age are likewise susceptible to this infection and supports the well-known clinical observation that while most cases of diphtheria occur among children from 1 to 5 years of age the disease is unfortunately by no means rare among infants.

TABLE 1.—THE TOXIN SKIN REACTION IN PERSONS OF VARIOUS AGES

| Age, Years | Total Tested | Reactions | | Per Cent. Positive |
|-------------|--------------|-----------|----------|--------------------|
| | | Positive | Negative | |
| Under 1 | 25 | 3 | 22 | 12 |
| 1-2 | 21 | 9 | 12 | 43 |
| 2-4 | 18 | 12 | 6 | 66 |
| 4-6 | 12 | 7 | 5 | 58 |
| 6-8 | 14 | 8 | 6 | 57 |
| 8-15 | 21 | 5 | 16 | 24 |
| 15-30 | 142 | 60 | 82 | 42 |
| Over 30 | 194 | 55 | 139 | 28 |
| Total | 447 | 159 | 288 | 41 |

TABLE 2.—PERCENTAGE OF PERSONS OF VARIOUS AGES SUSCEPTIBLE TO DIPHTHERIA *

| Age, Years | Percentage of Positive Toxin Reactions | | | Incidence of (14,000 cases) |
|------------|--|--------|--------|-----------------------------|
| | Park | Kolmer | Schick | |
| Under 1 | 40 | 12 | 7 | 3.2 |
| 1-5 | 65.9 | 54.5 | 53 | 45.4 |
| 5-10 | 42.5 | 57.8 | 50 | 32.2 |
| 10-15 | 26 | 24 | 50 | 8.1 |
| Over 15 | 33 | 35 | 10 | 11.4 |

* According to the toxin reaction and an analysis of 14,000 cases of diphtheria in the Philadelphia Hospital for Contagious Diseases.

The percentage of susceptible persons of various ages as shown by the toxin test is higher than statistics in diphtheria indicate; at least this is apparently true in Philadelphia (Table 2). Likewise the percentage of positive reactions observed by Schick, Park and ourselves, while in general about parallel, are somewhat discrepant, especially

among children from 1 to 5 years of age. We believe Dr. Park's figures are mainly based on observations among children suffering with scarlet fever, and this probably explains his higher percentage of positive reactions, for as we shall point out later, scarlet fever reduces resistance to diphtheria as indicated both by clinical data and a higher percentage of positive toxin reactions among persons with this disease.

It is but natural to expect the toxin reaction to show a higher percentage of susceptible persons than would be indicated by statistics in diphtheria, for many factors modify the infectiousness of the disease, as virulence of the bacillus, crowding, etc., and only under exceptional circumstances would one expect all susceptible persons exposed to diphtheria to contract the disease.

Cultures were made of the throats of a large number of persons tested, but there was no relation between the presence or absence of diphtheria bacilli and the toxin reaction. Natural antitoxic immunity cannot be ascribed to the presence of bacilli in the upper air-passages at least, with consequent stimulation of body cells and formation of antitoxin; at present there is apparently no satisfactory explanation to account for the production of natural antitoxin in some persons and its absence in others.

THE ANTITOXIN CONTENT OF THE SERUM OF PERSONS REACTING POSITIVELY AND NEGATIVELY TO THE TOXIN TEST

According to Schick, persons reacting positively to the toxin test usually contain less than one-thirtieth of a unit of antitoxin per cubic centimeter of serum. Park and his associates agree with this conclusion.

We have titrated the antitoxin content of the serums of a number of persons reacting negatively, weakly positively and strongly positively to the toxin test and give the results of some of these in Tables 3, 4 and 5. In some instances the results were indefinite and these have been omitted.

Technic.—For the purpose of measuring small amounts of antitoxin as fractions of a unit, Römer's intracutaneous method is generally employed.

We conduct this test as follows: An L + toxin is diluted 1:10 or 1:100, and from this stock dilution further dilutions are prepared with sterile normal salt solution. In a series of small sterile test-tubes are placed 0.2 c.c. of these varying dilutions of toxin and to these are added 0.2 c.c. of a solution of carefully standardized antitoxin each 0.1 c.c. of which contains $\frac{1}{1000}$ unit. The cotton stoppers of these tubes are paraffined to prevent evaporation, the contents of each tube are mixed by gentle shaking and all tubes incubated for an hour or two and then stood aside in a refrigerator over night.

Next morning 0.2 c.c. of each tube is injected intracutaneously in a guinea-pig (site prepared by pulling out the hairs). From three to five injections are made into the abdominal skin of one pig. The amount injected contains 0.1 c.c. of the toxin and 0.1 c.c. antitoxin ($\frac{1}{1000}$ unit); the balance is allowed for waste. The pigs are observed for three or four days and the toxin, which just produces roughening of the skin, is taken as the "limes-necrosis" (L_n) dose.

This determination having been made, varying amounts of the person's serum are mixed with this constant quantity of toxin and the tests conducted as described. If, for example, 0.002 c.c. of a patient's serum mixed with the L_n dose of toxin gave the same amount of necrosis in the same time as the identical quantity of the toxin with $\frac{1}{1000}$ standard unit, then 1 c.c. of this person's serum contains 0.5 unit.

TABLE 3.—ANTITOXIN CONTENT OF THE SERUMS OF PERSONS REACTING NEGATIVELY TO THE TOXIN TEST

| No. | Name | Age, Years | Antitoxin in Units per Cubic Centimeter of Serum |
|-----|--------|----------------|---|
| 1 | Dr. K. | 24 | 10 units. |
| 2 | Dr. R. | 36 | 10 units. |
| 3 | L. F. | 24 | About 1 unit. |
| 4 | M. L. | $\frac{7}{2}$ | About 10 units. |
| 5 | W. P. | $1\frac{1}{2}$ | About 10 units. |
| 6 | J. S. | 3 | About $\frac{1}{10}$ unit. |
| 7 | P. B. | 8 | About 4 units. |
| 8 | I. L. | $3\frac{1}{2}$ | From about $\frac{1}{30}$ to $\frac{1}{20}$ unit. |
| 9 | B. N. | 4 | From $\frac{1}{10}$ to 1 unit. |
| 10 | S. F. | 12 | About 10 units. |
| 11 | M. G. | 7 | 1 unit. |
| 12 | M. I. | 3 | About 6 units. |
| 13 | W. B. | 5 | About 2 units. |
| 14 | J. C. | 20 | From $\frac{1}{20}$ to $\frac{1}{10}$ unit. |
| 15 | B. M. | 6 | $\frac{1}{20}$ unit. |
| 16 | P. A. | 4 | $\frac{1}{20}$ unit. |
| 17 | C. H. | 7 | From $\frac{1}{10}$ to 1 unit. |
| 18 | F. H. | 2 | From 1 to 2 units. |
| 19 | M. A. | $1\frac{1}{2}$ | About $\frac{1}{10}$ unit. |
| 20 | B. B. | 8 | About 1 unit. |

We have obtained much better results, however, with the technic used by Park and Zingher.⁴ This consists in diluting a toxin so that 1 c.c. contains one-fortieth the L_+ dose. By mixing 0.2 c.c. of patient's serum with 0.2 c.c. of toxin, allowing to stand at room temperature for thirty minutes and injecting 0.1 c.c. of the mixture intracutaneously in the abdominal surface of a guinea-pig (prepared by pulling out the hairs) we are testing for one-fortieth unit of antitoxin to each cubic

4. Personal communication.

centimeter of serum. By using twice the quantity of serum we may test for one-eightieth unit and by so varying the quantities of serum and toxin in this manner the method is well adapted for determining quantities of antitoxin varying from 10 units to $\frac{1}{320}$ unit.

TABLE 4.—ANTITOXIN CONTENT OF THE SERUMS OF PERSONS REACTING WEAKLY POSITIVE TO THE TOXIN TEST

| No. | Name | Age, Years | Toxin Reaction Erythema in cm. | Antitoxin in Units per Cubic Centimeter of Serum |
|-----|--------|------------|--------------------------------|--|
| 1 | H. F. | 36 | 0.5×0.7 | From $\frac{1}{40}$ to $\frac{1}{20}$ unit. |
| 2 | Dr. M. | 24 | 0.3×0.5 | About $\frac{1}{80}$ unit. |
| 3 | E. F. | 30 | 0.6×0.4 | $\frac{1}{40}$ unit. |
| 4 | E. S. | 3 | 0.5×0.5 | $\frac{1}{40}$ to $\frac{1}{80}$ unit. |
| 5 | — G. | 25 | 0.5×0.5 | $\frac{1}{20}$ to $\frac{1}{10}$ unit. |
| 6 | C. S. | 10 | 0.4×0.7 | $\frac{1}{80}$ to $\frac{1}{40}$ unit. |
| 7 | A. M. | 5 | 0.3×0.6 | $\frac{1}{60}$ unit. |
| 8 | F. C. | 16 | 0.5×0.5 | About $\frac{1}{20}$ unit. |
| 9 | J. L. | 20 | 0.6×0.6 | About $\frac{1}{40}$ unit. |
| 10 | M. P. | 4 | 0.3×0.5 | $\frac{1}{80}$ to $\frac{1}{40}$ unit. |
| 11 | A. S. | 11 | 0.6×1.0 | $\frac{1}{10}$ unit. |
| 12 | A. M. | 8 | 0.5×0.8 | $\frac{1}{80}$ to $\frac{1}{40}$ unit. |

TABLE 5.—ANTITOXIN CONTENT OF THE SERUMS OF PERSONS REACTING STRONGLY POSITIVE TO THE TOXIN TEST

| No. | Name | Age, Years | Toxin Reaction Erythema in cm. | Antitoxin in Units per Cubic Centimeter of Serum |
|-----|--------|-----------------|--------------------------------|--|
| 1 | — B. | 21 | 1×1.5 | About $\frac{1}{40}$ unit. |
| 2 | — U. | 23 | 1×1.2 | $\frac{1}{40}$ to $\frac{1}{20}$ unit. |
| 3 | Dr. K. | 28 | 1.5×2.0 | None. |
| 4 | Dr. M. | 27 | 1.8×2.0 | About $\frac{1}{60}$ unit. |
| 5 | A. B. | 8 | 2.0×2.5 | None. |
| 6 | M. T. | 7 | 3.0×3.2 | None. |
| 7 | M. W. | 4 | 1.0×1.5 | $\frac{1}{60}$ to $\frac{1}{88}$ unit. |
| 8 | K. W. | 6 | 2.0×2.8 | None. |
| 9 | C. B. | 4 | 1.0×1.8 | About $\frac{1}{60}$ unit. |
| 10 | K. B. | 2 $\frac{1}{2}$ | 1.5×1.8 | $\frac{1}{80}$ to $\frac{1}{40}$ unit. |

We generally make from two to four inoculations in each pig at the same time; thus with the serum of a person reacting negatively we may test for $\frac{1}{20}$ and $\frac{1}{10}$, or 1 and 2 units simultaneously.

The pigs are observed for three or four days when the results are recorded. Distinct roughening of the skin with superficial necrosis is regarded as positive and indicating incomplete neutralization. The injection of serum alone may leave a small nodule, but the skin over



The Schick test for immunity in diphtheria. Dr. J. A. K., a well-marked reaction thirty-six hours after the intracutaneous injection of one-fortieth the minimum lethal dose of a diphtheria toxin diluted to 0.05 c.c. The patient's blood contained no antitoxin. The brownish erythematous area with edematous infiltration of the subcutaneous tissues are characteristic of the reaction.

it is smooth. Park and Zingher advise heating fresh serums to 55 C. for half an hour before testing in order to prevent or reduce this knob-like lesion. We have not found this generally necessary.

An examination of these tables shows the following:

1. The serums of persons reacting negatively to the toxin test usually contain at least $\frac{1}{20}$ unit of antitoxin per cubic centimeter of serum. In one instance about $\frac{1}{30}$ unit was found. This agrees quite closely with the results of Schick and Park, who found that $\frac{1}{30}$ unit was usually sufficient to neutralize the toxin. Probably the slight difference in our results is due to the fact that we use one-fortieth instead of one-fiftieth of the minimum lethal dose as the amount of toxin injected.

2. It is interesting to note that the serums of 5 per cent. of persons tested contained at least 10 units of antitoxin per cubic centimeter of serum. It may be that the antitoxin content of some of these was still higher, but our titrations were not continued beyond this determination.

3. The serums of persons reacting weakly positive to the toxin test usually contained from $\frac{1}{40}$ to $\frac{1}{160}$ unit of antitoxin per cubic centimeter. In one instance as much as $\frac{1}{10}$ unit was found and in several others about $\frac{1}{20}$ unit.

4. The serums of persons reacting strongly positive were found to contain less than $\frac{1}{20}$ unit per cubic centimeter of serum and frequently none at all could be detected.

THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA AS STUDIED BY THE TOXIN SKIN TEST

Clinical experience with diphtheria antitoxin as an immunizing agent has long since taught that sufficient passive immunity to insure adequate protection does not usually persist over three or four weeks, and not infrequently is of much shorter duration. For this reason efforts are being made to perfect a method of active immunization with toxin-antitoxin mixtures, because the antitoxin produced by our own body cells persists in the body fluids for longer periods of time.

We have applied the toxin test to 108 children varying in age from 2 months to 3 years, all of whom had received 1,250 units of antitoxin by subcutaneous injection at varying intervals of time prior to the tests. The results are shown in Table 6. Most of these children were feeding cases or convalescents and only a few were suffering with an acute infection as broncho-pneumonia.

Among children from 2 months to 3 years of age a positive toxin reaction could be expected in about 40 per cent. It is of interest to note that the immunity conferred by 1,250 units of antitoxin, equal

approximately to 100 to 400 units per kilo of body weight, was apparently efficient for ten days; after this interval antitoxin rapidly disappeared, so that after four to six weeks the immunity may be regarded as having entirely disappeared.

TABLE 6.—THE TOXIN SKIN REACTION IN CHILDREN WHO HAD RECEIVED 1,250 UNITS OF ANTITOXIN

| Days After Injection of Antitoxin | Total | Toxin Skin Reaction | | Per Cent. Positive |
|---|-------|---------------------|----------|-----------------------|
| | | Positive | Negative | |
| 1-5 | 10 | 0 | 10 | 0 |
| 5-10 | 18 | 0 | 18 | 0 |
| 10-20 | 12 | 3 | 9 | 25.0 |
| 20-30 | 14 | 4 | 10 | 28.5 |
| 30-50 | 36 | 13 | 23 | 36.1 |
| Over 7 weeks | 16 | 7 | 9 | 43.7 |
| Total | 106 | 27 | 79 | |

TABLE 7.—THE TOXIN SKIN REACTION IN SCARLET FEVER PATIENTS WHO HAD RECEIVED 2,500 UNITS OF ANTITOXIN BY SUBCUTANEOUS INJECTION

| Days After Antitoxin | Total | Toxin Skin Reaction | | Per Cent. Positive |
|-------------------------|-------|---------------------|----------|-----------------------|
| | | Positive | Negative | |
| 1-5 | 60 | 2 | 58 | 3.3 |
| 5-10 | 45 | 3 | 42 | 6.6 |
| 10-20 | 65 | 9 | 56 | 13.9 |
| 20-30 | 77 | 17 | 60 | 22.0 |
| 30-40 | 50 | 17 | 33 | 34.0 |
| 40-50 | 37 | 21 | 16 | 56.7 |
| Over 50 | 28 | 19 | 9 | 67.8 |
| Total | 362 | 88 | 274 | |

THE DURATION OF PASSIVE IMMUNITY TO DIPHTHERIA AMONG PERSONS
SUFFERING WITH SCARLET FEVER AS STUDIED BY
THE TOXIN SKIN TEST

As is well known, persons suffering with scarlet fever are rendered peculiarly susceptible to diphtheria, especially from the third to the sixth week of the disease. Cases of postscarlatinal diphtheria are much more common in hospital than in private practice, as it occasionally happens that in a large hospital ward cases of secondary diphtheria remain undetected and expose other patients to the infection. Further than this, it would appear that during the early stages

of scarlet fever natural immunity to diphtheria is reduced as it is to streptococcus infection.

We have applied the toxin skin test to 362 persons in the various stages of scarlet fever and at varying intervals of time following the subcutaneous injection of 2,500 units of antitoxin. As the antitoxin is administered as a routine measure within from twelve to twenty-four hours after admission to the hospital, the stage of the disease may be estimated in the table according to the number of days after the injection of serum. With the exception of a few adults, all of these patients were from $2\frac{1}{2}$ to 14 years of age.

When compared with Table 6 it will be found that in *scarlet fever passive immunity following the injection of diphtheria antitoxin is of shorter duration than that induced among approximately normal children, in that 10 per cent. of the former are susceptible within ten days after receiving antitoxin.* Whether this is due to accelerated elimination of the horse-serum antitoxin during the acute stages of scarlet fever or to other causes we are unable to state.

This increased susceptibility to diphtheria among scarlet fever patients is also shown in Table 8, compiled from the results of toxin tests among children of the same age.

TABLE 8.—PERCENTAGE OF POSITIVE TOXIN REACTIONS AMONG NORMAL CHILDREN AND CHILDREN WITH SCARLET FEVER*

| | Days | | |
|--|------|-------|-------|
| | 1-10 | 10-20 | 20-60 |
| Percentage of positive reactions in normal children after 1,250 units of antitoxin..... | 0 | 25 | 36 |
| Percentage of positive reactions in children with scarlet fever after 2,500 units antitoxin..... | 3 | 20 | 36 |

* Children aged 1 to 8 years.

Cultures of the throat were made in all of these cases, but there was no relation between the percentage of carriers and positive toxin reaction. Thus 46 of these persons showed the presence of diphtheria bacilli mostly of the solid types; of these, 10 gave a positive and 36 a negative toxin reaction.

A STUDY OF IMMUNITY DURING AND FOLLOWING AN ATTACK OF DIPHTHERIA BY MEANS OF THE TOXIN SKIN TEST

We have applied the toxin skin test to 350 persons, mostly children, suffering with diphtheria and receiving antitoxin treatment. This study was of much interest for two reasons:

1. From the possibility of throwing some light on the question of dosage of antitoxin.
2. To determine the degree of immunity induced as a result of active stimulation of body cells by the diphtheria toxin of the patient's infection.

All these patients were being treated in the diphtheria department of the Philadelphia Hospital for Contagious Diseases. Antitoxin was given in doses varying from 10,000 to 100,000 units, the average being 45,000 units, by subcutaneous injection. The patients were mostly children from 2 to 15 years of age. As a general rule, the first dose of antitoxin was given during the first forty-eight hours of the infection. The results of the toxin skin tests are summarized in Table 9.

TABLE 9.—THE TOXIN SKIN REACTION AMONG PERSONS SUFFERING WITH DIPHtheria AND RECEIVING ANTITOXIN

| Days After Antitoxin | Total | Toxin Skin Reaction | | Per Cent. Positive |
|----------------------|-------|---------------------|----------|--------------------|
| | | Positive | Negative | |
| 1-5 | 81 | 14 | 67 | 17.2 |
| 5-10 | 86 | 22 | 64 | 25.5 |
| 10-20 | 96 | 33 | 63 | 34.3 |
| 20-30 | 40 | 14 | 26 | 35.0 |
| 30-50 | 28 | 13 | 15 | 46.4 |
| Over 50 | 19 | 13 | 6 | 68.4 |
| Total | 350 | 109 | 241 | |

As shown in this table, a rather large proportion of patients reacted positively, especially within the first ten days of the disease and after receiving antitoxin. Among children of the ages of these patients a positive toxin reaction could be expected in from 40 to 50 per cent. As shown in the tables, these patients were in general just as susceptible after an attack of diphtheria as before; in other words, it would appear that the body cells produced little or no homologous antitoxin and the immune antitoxin is soon eliminated. This has an important bearing on the use of T-A mixtures in active immunization and indicates that antitoxic immunity is acquired only with prolonged stimulation of the body cells.

As stated, the high percentage of positive reactions during the first ten days of the disease and after large doses of antitoxin was quite surprising. As a general rule, these occurred among children with severe infections. We have listed a few of these in Table 10.

It is difficult to find an explanation for the relatively high percentage of positive reactions so soon after large doses of antitoxin. Naturally, one may suppose that the immune antitoxin is quickly neutralized so that the toxin injected intracutaneously is not neutralized. This supposition receives some support in view of the observation that most, not all, of the positive skin reactions occurred among those

with severe infections, as if heavy toxin production at the site of infection neutralized the large amount of antitoxin administered. If this is true, the claim that large doses of antitoxin are required in the treatment of diphtheria receives support.

TABLE 10.—THE TOXIN SKIN REACTION AMONG PERSONS SUFFERING WITH DIPHTHERIA AND RECEIVING ANTITOXIN

| No. | Age, Years | Diagnosis | Antitoxin Units | Days After Antitoxin | Positive Toxin Reaction (cm.) |
|-----|------------|--------------------------|-----------------|----------------------|-------------------------------|
| 54 | 2 | Tonsillar diphtheria. | 23,000 | 3 | 2×1.5 |
| 55 | 10 | Tonsillar diphtheria. | 20,000 | 4 | 1×0.5 |
| 107 | 7 | Tonsil. and Laryn. diph. | 50,000 | 6 | 0.3×0.4 |
| 3 | 5 | Tonsil. and Laryn. diph. | 50,000 | 8 | 1×1.0 |
| 61 | 10 | Tonsillar diphtheria. | 60,000 | 8 | 2×2.0 |
| 65 | 15 | Tonsil. and Laryn. diph. | 175,000 | 8 | 2×2.5 |
| 69 | 6 | Tonsillar diphtheria. | 40,000 | 8 | 1×0.6 |
| 87 | 15 | Tonsil. and Laryn. diph. | 75,000 | 6 | 1×1.2 |
| 100 | 3 | Tonsil. and Laryn. diph. | 45,000 | 8 | 0.4×0.5 |
| 106 | 5 | Tonsil. and Laryn. diph. | 30,000 | 9 | 0.6×0.5 |
| 68 | 7 | Tonsillar diphtheria. | 30,000 | 11 | 1.5×1.5 |
| 16 | 13 | Tonsil. and Laryn. diph. | 60,000 | 13 | 0.5×0.6 |
| 43 | 8 | Tonsillar diphtheria. | 40,000 | 13 | 1×1.2 |
| 23 | 5 | Tonsillar diphtheria. | 23,000 | 15 | 1×1.0 |
| 6 | 8 | Tonsil. and Laryn. diph. | 50,000 | 18 | 1×1.2 |
| 1 | 5 | Tonsil. and Laryn. diph. | 35,000 | 19 | 1×1.0 |
| 30 | 3 | Tonsillar diphtheria. | 30,000 | 19 | 1×1.0 |
| 36 | 2 | Tonsil. and Laryn. diph. | 30,000 | 17 | 0.5×0.6 |
| 18 | 9 | Tonsil. and Laryn. diph. | 45,000 | 16 | 1.5×2.0 |
| 44 | 7½ | Tonsillar diphtheria. | 45,000 | 13 | 1×1.2 |

PRACTICAL VALUE OF THE TOXIN SKIN REACTION

On the assumption that a negative toxin reaction indicates that an individual possesses sufficient immunity to diphtheria to afford protection in case of exposure, the chief practical value and application of this test would be for the purpose of detecting non-immune individuals and immunizing these only instead of all persons indiscriminately. This not only would prove of importance from the point of view of economy, but also would spare many persons the discomfort of an injection of serum and consequent sensitization by horse protein.

We have had one experience that has greatly increased our confidence in the practical value of this toxin reaction. During the past year a nurse in the Polyclinic Hospital contracted diphtheria and was sent for treatment to the Philadelphia Hospital for Contagious Diseases. Within forty-eight hours the toxin skin test was applied to all nurses as well as resident physicians, patients and attendants in the Polyclinic Hospital. All nurses reacting positively were given 2,500 units of antitoxin by subcutaneous injection. Those reacting negatively were not immunized.

Within two weeks five nurses contracted diphtheria and all of these were among those who had shown a positive skin test and had received antitoxin. None of those persons reacting negatively to the skin test contracted the disease. The first nurse sent to the hospital to aid in nursing contracted diphtheria; unfortunately a toxin test had not been made in her case. A second nurse who reacted negatively was sent to the hospital to aid in the care of the infected nurses; she did not receive a prophylactic injection of antitoxin and did not contract the disease. Later one of the nurses reacting negatively to the toxin test complained of sore throat and inspection showed redness of the fauces and a few spots of exudate on one tonsil; a series of cultures showed the presence of streptococci and staphylococci, but no diphtheria bacilli. In a few days the patient was again on duty.

One of the patients who reacted negatively showed diphtheria bacilli in the throat which were virulent for guinea-pigs; for this reason the patient was removed to the hospital under the assumption that he may be a dangerous carrier. There were absolutely no clinical evidences of diphtheria.

While we must wait several years during which the reaction may be tried under similar circumstances before a final verdict of its practical value may be expressed, we believe that this test will prove quite reliable as a guide in determining which persons should be immunized under conditions of exposure. This is especially true in institutions as hospitals, asylums and the like. The test also finds ready application in private practice and since additional evidence at hand indicates that a person reacting negatively tends to react similarly for an indefinite period, physicians may test children at intervals to determine the state of their resistance to diphtheria.

In the presence of an outbreak of diphtheria therefore, the physician should take cultures and apply the toxin test to all persons exposed. At the end of twenty-four hours he has the evidence offered by both at hand. *This delay of twenty-four hours before immunizing with antitoxin is justifiable unless a contact shows clinical signs suggestive of diphtheria. In such an instance we believe that antitoxin should be given at once.*

The reaction has a special field of usefulness in hospitals and wards for the care of children. All children should be subjected to the toxin test prior to admission and those immunized who react positively. If it is the custom to reinject with antitoxin a month or six weeks later it is better practice to apply the toxin test first and administer serum to those only who show a positive reaction. This means a saving of antitoxin and the avoidance of disagreeable serum sickness.

The toxin test will probably not prove of value in handling the difficult problem of the diphtheria carrier. Our experiences with this class of cases may be summarized as follows:

A. Persons may harbor in the upper air-passages diphtheria bacilli virulent for guinea-pigs and react negatively to the toxin test. Presumably the absence of both symptoms and reaction are due to the presence of antitoxin in the blood serum. One such person had about 5 units of antitoxin per cubic centimeter of his serum. While such persons may be in apparent good health, nevertheless they constitute a danger to others.

B. Several diphtheria convalescents harboring bacilli virulent for guinea-pigs reacted positively to the skin test, but showed no clinical evidences of diphtheritic intoxication.

C. In a number of instances bacilli that proved non-virulent for guinea-pigs have been isolated from the throats, noses and ears of persons reacting positively to the toxin test. As already stated, we have found no relation between the toxin reaction and the percentage of diphtheria bacilli carriers; in the majority of such instances it is probable that the bacilli are harmless. Park and his associates have employed the test in scarlet fever patients, and while more than one-fourth of those reacting negatively became carriers no cases of clinical diphtheria developed among them.

Apparently, there is but one reliable means of determining the disease-producing powers of a given culture of diphtheria bacilli, namely, the guinea-pig inoculation test. *In the absence of clinical signs and symptoms the toxin reaction offers no aid in this direction.* In persons showing some clinical evidences of an infection, particularly a dirty nasal discharge containing diphtheria-like bacilli, or a tonsillitis showing staphylococci or streptococci and a diphtheria bacillus, we are inclined to agree with Park that the toxin test may possess some diagnostic value. If the person reacts negatively, diphtheria may be excluded on the basis that antitoxin in the blood-serum sufficient to effect neutralization of the test toxin will protect the individual against diphtheria; on the other hand, a positive reaction indicates that diphtheria is still a probability on the basis that the individual is shown to be at least susceptible to the infection.

It is to be remembered that a person reacting positively will not necessarily contract diphtheria even though exposed. Of twenty-five nurses and attendants in the scarlet fever department of the hospital, no less than sixteen reacted positively; many of these have been exposed to diphtheria many times during a period of several years and have received no antitoxin and nevertheless have escaped infection.

SUMMARY

1. The toxin skin reaction is a valuable and reliable method for detecting susceptibility to diphtheria.

2. Persons reacting negatively to this test usually contain at least $\frac{1}{20}$ unit of diphtheria antitoxin per cubic centimeter of serum, and this amount of antitoxin is probably sufficient to protect against infection.

3. Persons reacting weakly or strongly positive usually contain less than $\frac{1}{40}$ of a unit of antitoxin per cubic centimeter of serum or none at all. These persons may be regarded as susceptible to diphtheria and in the event of exposure to infection should be passively immunized with an injection of antitoxin.

4. About 40 to 50 per cent. of children ranging from 1 to 15 years of age react positively to the toxin test; this means that the preliminary use of the toxin test will eliminate the necessity of administering prophylactic doses of antitoxin to about 50 per cent. of children.

5. The toxin reaction indicates that the immunity conferred by an injection of antitoxin begins to disappear after ten days and has generally passed away entirely after four weeks.

6. The increased susceptibility of persons with scarlet fever to diphtheria is shown by the toxin reaction; even after the injection of antitoxin about 10 per cent. are susceptible within ten days.

7. According to the toxin reaction the immunity conferred by an attack of diphtheria is usually of short duration or entirely absent.

8. The most practical application of the toxin reaction consists in applying the test as a preliminary measure to all persons who have been exposed to diphtheria and immunizing only those who react positively.

We wish to express our thanks to Dr. S. McC. Hamill, Dr. J. P. C. Griffith, Dr. W. Hollopeter, Dr. A. Eshner and other physicians for the clinical opportunities afforded us in various Philadelphia hospitals.

Second and Luzerne Streets.

BLUE SCLEROTICS ASSOCIATED WITH BRITTLE BONES

REPORT OF A CASE IN A CHILD TWO YEARS OLD *

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Blue-tinged sclerotics are not infrequently seen in infants and young children. In tuberculous patients also such a blue tinge may occasionally be noted. Congenital heart disease with marked cyanosis may be associated with blue sclerotics, and is largely due to venous congestion. In negro infants and children I have sometimes noted patches of pigmentation in the sclerotics. The blue sclerotics which I am about to describe are entirely distinct from any of these. The condition is congenital and the sclerotics are of a uniform blue color. The first to note the peculiarity was von Ammon;¹ his description is as follows:

Congenital diseases of the sclerotic are rare. . . . Of importance is a peculiar whitish blue coloration of this membrane occasionally met with when the whole development of the eye is retarded. The sclerotic in such cases appears thin and almost transparent. I have seen it also in congenital hydrophthalmus. . . . A similar thinness occurs in patients suffering from congenital heart disease. In that case the sclerotic is dark blue, this being due partly to the thin condition of the membrane and partly to an accumulation of venous blood and a large mass of pigment in the eye.

In 1903 Buchanan² made the first microscopic examination and found:

The cornea and sclerotic were unusually thin, the cornea being three-fifths and the sclerotic one-third of its normal thickness. Histological examination showed that the fibers of the cornea and sclerotic were of about normal size, but unusually few in number. The anterior elastic lamina was entirely absent.

The hereditary transmission of blue sclerotics was first pointed out by Peters³ in 1908. He reported cases occurring in four generations. Four of his patients also showed a typical embryontoxon.⁴

* Received for publication Jan. 1, 1915.

* Read before the Section on Ophthalmology, the New York Academy of Medicine, Jan. 18, 1915.

1. Von Ammon: *Darstellungen der Krankheiten und Bildungsfehler des menschlichen Auges*, 1841, iii, 73.

2. Buchanan: *Tr. Ophthal. Soc. U. Kingdom*, 1903, xxiii, 267.

3. Peters: *Klin. Monatsbl. f. Augenh.*, 1908, p. 130; *Die angeborenen Fehler und Erkrankungen des Auges*, 1909, p. 80.

4. An extension of the upper layers of the sclerotic into the cornea. Pressure of the lids is said to cause accentuation at the upper and lower corneo-sclerotic margin.

Peters also regarded the condition as due to an abnormally thin or abnormally transparent sclerotic. In 1910 Stephenson⁵ described a series of twenty-one cases occurring in four generations of one family. In two cases the presence of an arcus senilis or an embryontoxon was noted. Subsequent investigation enabled Harman⁶ to add another generation to this family, so that of a total of fifty-five members, thirty-one showed the same congenital peculiarity with some slight individual differences. By referring to Figure 1, it will be seen that the condition is transmitted only through affected members; it never skips a generation, and no members with white sclerotics transmit blue sclerotics to their offspring. About 50 per cent. of the children born to parents with blue sclerotics show the anomaly.

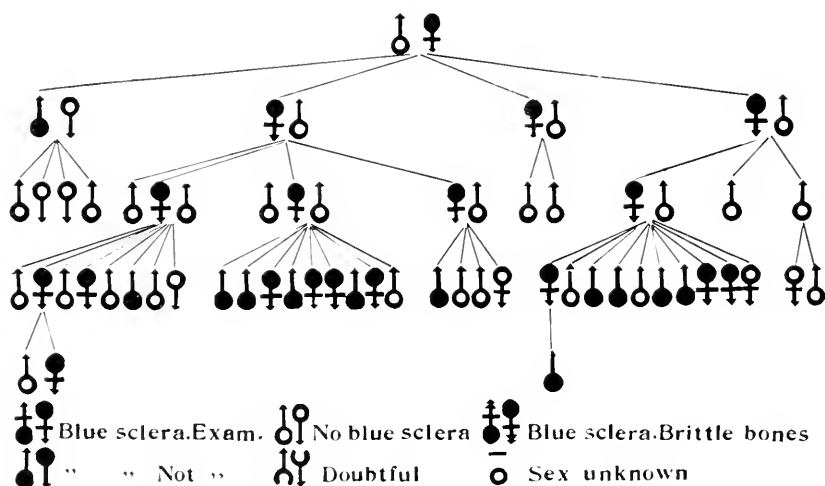


Fig. 1.—Chart of Stephenson and Harman's series of cases of blue sclerotics.

The first author to mention the association of blue sclerotics with brittle bones was Eddowes.⁷ In 1900 he published a brief report on "Dark Sclerotics and Fragilitas Ossium," in which he described a case in a young woman whose father also had a similar condition. He mentions having seen some years previously a boy with blue sclerotics who in the course of two years during which he was under observation had nine fractures.

In 1911 Burrows⁸ reported a series of cases occurring in four generations of one family, in which, of twenty-nine individuals,

5. Stephenson: *Ophthalmoscope*, 1910, viii, 330.

6. Harman: *Ophthalmoscope*, 1910, viii, 559.

7. Eddowes: *Brit. Med. Jour.*, 1900, ii, 202.

8. Burrows: *Brit. Med. Jour.*, 1911, ii, 16.

thirteen had blue sclerotics and nine of those fractures also (Fig. 2). Of these nine, seven had multiple fractures.

In 1912 Adair-Dighton⁹ published a report of four generations of blue sclerotics; of thirty-two individuals, twenty-one had blue sclerotics (Fig. 3), and several of these brittle bones. During the last two years cases have also been reported by Conlon,¹⁰ Cockayne¹¹ and Ostheimer.¹² Rolleston's¹³ case, which was associated with congenital syphilis, probably belongs to this group.

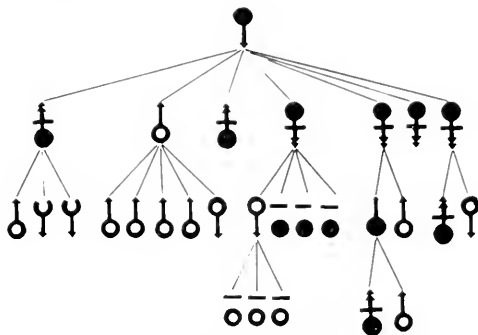


Fig. 2—Chart of Burrows' series of cases of blue sclerotics associated with fragility of bones.

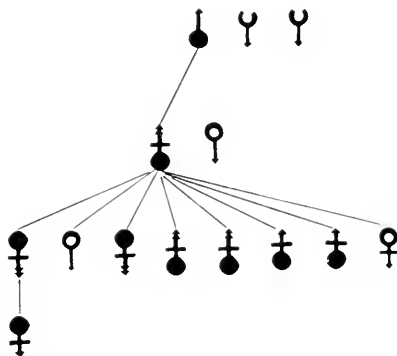


Fig. 3.—Chart of Adair-Dighton's series of cases of blue sclerotics associated with fragility of bones.

REPORT OF CASE

The following is a brief account of a boy of 2 years whom I have recently observed:

The patient was first seen in February, 1914, at the age of 20 months. The parents are apparently healthy, but the father is rather small and thin, weighing only 120 pounds; the mother is of average size and robust. As far as the

9. Adair-Dighton: *Ophthalmoscope*, 1912, x, 188.

10. Conlon: *Boston Med. and Surg. Jour.*, 1913, clxix, 16.

11. Cockayne: *Ophthalmoscope*, 1914, xii, 271.

12. Ostheimer, Maurice: *Fragilitas Ossium*, *Jour. Am. Med. Assn.*, Dec. 5, 1914, p. 1996.

13. Rolleston: *Brit. Jour. Child. Dis.*, 1911, p. 202.

parents know, no other members of the family have had blue sclerotics or brittle bones. There were no miscarriages; no evidence of syphilis or other constitutional disease. The parents have been married eleven years and have three children besides the patient. Two of these children I have examined and found perfectly normal. They began to walk and talk at the proper age. The patient was born normally and nursed for ten months. The first teeth appeared at 8 months, and the child began to sit up at 9 months. At 20 months (February, 1914) he was not yet able to stand or to talk distinctly. In December, 1913, he fell from an ordinary chair and fractured his right tibia, and six weeks later while in bed with the cast still applied, he sustained a fracture of the right femur. He began to walk at 23 months and now at $2\frac{1}{2}$ years can say



Fig. 4.—E. G., aged 30 months; blue sclerotics associated with brittle bones.

short sentences. Physical examination on Dec. 16, 1914, aged 30 months, shows (Fig. 4) a small, thin, fair-haired boy distinctly below the normal, both physically and mentally. Height 32 inches (81 cm.), weight 22 pounds.

| Patient | | Normal |
|---------------------------------|--------|----------|
| Head—Biparietal, diameter | 14 cm. | 13.5 cm. |
| Above the ears, diameter..... | 13 cm. | 12 cm. |
| Occipitofrontal, diameter | 17 cm. | 17 cm. |
| Circumference of head | 51 cm. | 48.5 cm. |
| Circumference of chest..... | 48 cm. | 49.7 cm. |
| Circumference of abdomen..... | 47 cm. | |

The head is large and brow prominent, the fontanel closed. The sclerotics are of a distinct peculiar blue color throughout. The patient has sixteen teeth. There are no signs of rickets, no rosary, no enlargement of the epiphyses. The examination of the chest is negative. There is no congenital heart dis-

ease. Radiographic examinations of the legs and arms were made. In the patient I employed a method which I have used for a number of years. The extremity of the patient was taken with that of a normal child of the same age at the same time on the same plate. In this way even those not accustomed



Fig. 5.—Right femur and tibia (A) of E. G., aged 18 months; taken on same plate at same time of femur and tibia (B) of normal infant of 18 months.

to interpret plates will have no difficulty in detecting differences in structure. It will be seen (Fig. 5) that all trace of the fracture has disappeared. Comparing the two bones, it will be noted that in length and thickness they are about the same, but one is far more transparent and lacks density. It is deli-

cate in structure especially towards the proximal end of the tibia; hardly any cortical portion is seen; the epiphyseal ends are broadened and show a distinct lack of cortical substance. Not only the bones but also the soft parts, the muscles and ligaments show the same lack of density, which indicates a diminished amount of fibrous tissue. The roentgenogram of the arm, in striking contrast to that of the leg, shows very little change from the normal (Fig. 6).

The patients affected with this combination of blue sclerotics and brittle bones are usually small and delicate, frequently fair-haired. The large size of the head is mentioned in several cases. Whether the intelligence is slightly retarded in many cases I cannot say. In my own patient his inability to run and play with other children may have had something to do with the matter. In another patient whom I saw through the courtesy of Dr. Reitzfeld, a boy of fifteen years, the intelligence was apparently normal.

The color of the sclerotic varies in different individuals from a pale azure or porcelain blue to a leaden hue. The color is uniform throughout and involves the entire sclerotic from the cornea as far as the eye



Fig. 6.—Hand and arm of E. G., aged 30 months.

ball is visible. According to Rolleston, the color is more distinct on some days. Usually there is no accentuation in the ciliary zone, but Harman mentions one case in which the color was deeper in the ciliary region and masked toward the equator on account of the increased thickness of the overlying conjunctiva, and also masked in those regions in which the muscle tendons overlay the globe. As was pointed out by Buchanan and others, the fibrous tissue is abnormally thin; the individual fibers are of normal thickness, but are deficient in number. The cornea is thin and the anterior elastic lamina is absent, which is said to account for the astigmatism frequently present in these patients. The choroid is also abnormally thin, which causes Fuchs' coloboma and the oval appearance of the optic disks (Stephenson, Harman). As to the bones, there seems to be a defect in the quality and quantity of fibrous tissue forming the framework which causes a lack of elasticity and the tendency to fracture. This change is well shown in the radiographs, and, as has been pointed out, not only the bones, but also the soft parts are also affected so that sprains are not infrequent. I

have no doubt that a careful examination will reveal changes in structure and a lack of fibrous tissue in other parts of the body. The change in the eye is so apparent that it would naturally be the first part noticed. According to Ostheimer,¹² of thirty-two patients with "fragilitas ossium" who were able to go about, only six were noted to have blue sclerotics, but I have no doubt that in a few other cases the peculiar color of the eye may have been overlooked. Not all patients who have blue sclerotics have brittle bones, but in the families in which blue sclerotics was an inherited peculiarity, all those members who had brittle bones had blue sclerotics also. The blue sclerotics like the fragility of the bones, may, however, occur independently of hereditary transmission. Ostheimer¹² states that in only eight of 117 cases of "fragilitas ossium" was the condition known to exist in either parent and in only twenty-four was it present in brothers or sisters.

COMMENT BY DR. FRIDENBERG

Ophthalmologic examination of the little boy with blue sclerotics shows no abnormality of the eyes beyond just this peculiar condition. The color of the sclerae is uniform, as far back as it can be seen. I should call it a Delft or china blue, as it has a decidedly grayish cast. I also notice a peculiar leaden-gray color of the iris, like that seen in the newly-born, and think this may be of significance. I am not aware that it has been noted by previous observers in these cases, and will refer to its causation later on. The vision seems acute, and there is but slight ametropia. The child was very restless, and I could, at best, make out a general hyperopic refraction. The fundus was not deeply pigmented, in contrast to the case examined by Stephenson. In fact, I should call it very blond if not suggesting, at least, albinism. The disks were perfectly normal in appearance and of the usual size and shape. I might mention here that the congenital crescent downward or Fuchs' coloboma was seen in but one of these cases, and is occasionally noted in otherwise perfectly normal eyes. I do not think it has any significance for us.

As to these blue sclerotics, it was early recognized that they are due, not to any actual pigmentation, but to the unusually translucent sclera allowing the brown-black choroid to shine through, as it were, producing a color interference. That a thinning is the principal cause of this optical condition is, I think, disproved by the fact that there was in all these cases, say more than fifty, no mention of sclerectasia or of a distention of the globe in the form of infantile glaucoma or hydrophthalmos, and no ophthalmoscopic evidence in any case, of a giving way at the posterior pole (coloboma, posterior staphyloma). The condition quoted from Ammon is, as indicated in the title, some-

thing quite different, namely, a case of true infantile glaucoma or hydrophthalmus with marked thinning of the sclera, and consequent bluish translucency.

To come back to the peculiar lead-gray iris in this case, the normal color of this membrane ordinarily depends on color interference, the brown-black of the posterior or pigment layer shining through more or less as the pigment in the stroma is absent, scanty or marked. Where the pigment is entirely absent we get a light gray-blue iris which is translucent, the pink or rabbit eye of albinism. The marked transparency of both sclera and iris, in spite of an apparently normal or but slightly reduced thickness, is, I believe, due merely to absence of lime salts in the connective tissue elements of these structures. Lime salts are the deposits which as we know produce opacities in the ocular media which appear white to reflected light. Transillumination did not show any remarkable difference from the normal eye, and this again, I think, indicates that there is at least no excessive thinning of the sclera. I doubt, too, very much, whether there is in most or in any of these cases an actual absence of the anterior elastic lamina or of any other layer of the cornea, as such a condition occurring in early life would, I am sure, give rise not only to astigmatism, but to marked keratoglobus or conical cornea if not to even more decided developmental anomalies.¹⁴

The following passage in Dr. Herrman's paper is significant: "Not only the bones but the soft parts, the muscles and ligaments show the same lack of density, which indicates a deficient amount of fibrous tissue." If we lay stress on the defective quality, that is, lack of lime salts, of actual calcification and ossification, rather than on the amount of fibrous tissue, I think we shall be more nearly right. This is indicated by the roentgenograms of the fragile bones, which were found to be of about normal length and thickness. It is probable, as this passage suggests, that all connective tissue throughout the body is lacking in density, and it would be interesting to examine, among other structures, the nails, teeth and hair for further evidence of this anomaly.

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14. The correctness, or rather, the applicability of Buchanan's findings have been questioned (see Conlon).

THE CHEMICAL COMPOSITION OF DIARRHEAL AS COMPARED WITH NORMAL STOOLS IN INFANTS *

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It has been a matter of considerable surprise on going through medical literature to see how little has been written regarding the chemical composition of diarrheal as compared with normal stools. Stools of all varieties have been studied in many ways in great detail since the work of Uffelmann and Wegscheider about forty-five years ago. Numerous reports have been published of metabolism work which contain stool analyses made with reference to the different constituents, fat, nitrogen, ash, etc.; and scattered through these are found reports of isolated instances in which very loose stools have been studied, but, so far as we are aware, no attempt has been made to correlate the observations on diarrheal stools and compare them with those which were normal. The work done on diarrheal stools as such has been chiefly a study of the flora.

It was with the belief that some new light might possibly be thrown on the treatment of such conditions, dietetic and otherwise, that we have made from another point of view a restudy of our metabolism observations, namely, to determine the actual chemical composition of diarrheal stools and compare them with the normal.

Those whose observation on infants' stools is limited to an inspection of napkins can form but an imperfect idea of even the gross condition of the infants' excretions, especially as to the amount of water which they contain. When stools are received in a metabolism basin a very different impression is made.

With the two large factors in the production of loose stools, that is, increased secretion and increased peristalsis, every one is familiar. But many questions arise relating to diarrheal stools. Do very loose stools differ from normal ones only in that they contain more water, or do they actually represent a much greater loss of solids? Are all the solids in the stool affected to the same degree, or are some drained

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* From the Laboratories of the Babies' Hospital and the Rockefeller Institute.

away much more than others? Does the actual loss, or the percentage of intake lost, vary only with the food, or are there other important factors?

These were some of the questions regarding which it was thought information might be gained by such a study as that undertaken. The data have been derived by going through the records of our metabolism studies for the past four years and selecting from them the cases illustrating the different types of stools. Such records were especially valuable for our purpose, for, although the children studied differed considerably with respect to their condition and the food given, the exact intake of the different food elements had been determined, as well as the composition of the excretion. In a few of the early cases the stool analysis did not go further in the ash estimation than to determine the total ash; but in all the recent ones, including the greater number studied, the composition of the ash had been fully worked out.

While the chemical composition of the stools was much influenced by the food, it did not seem to make much difference what the exciting cause of the diarrhea happened to be, as its effect in draining away fluids and solids from the body was much the same in all cases studied.

For the purpose of this study the cases were divided into (A) formed, firm or pasty stools; (B) loose stools and (C) very loose stools. The division into loose and very loose is a somewhat arbitrary one. We classed as "loose" those in which the total quantity of water lost varied between 100 and 200 c.c. daily; as "very loose" those in which the water exceeded 200 c.c. daily.

No account was taken of the number of evacuations during the day, first, because in metabolism observations this is somewhat difficult to determine, and secondly, for the reason that it is really of little importance. What is essential is the total daily excretion.

In the group A, of stools of normal consistency and appearance, there were observations made on 9 patients for 11 periods. In the group B, loose stools, there were observations made on 8 patients for 14 periods. In the group C, very loose stools, observations were made on 6 patients for 10 periods. In all, observations were made on 21 patients for 35 periods, for a total of 128 days.

A different period signifies an observation on the same child at another time or on another food. In all but two instances each period was for a longer time than a single day; usually it was three or four days. This was found convenient and sometimes necessary, since in estimating some of the salts of the ash, of which the quantity was very small, the total secretion of two or three days was needed for a satis-

factory quantitative determination. The amounts of the substances given in the table represents an average for the period. Two or three days were put in the same period only when the food was the same and the stools similar in character. In all cases daily averages of all the observations are given in the charts, and in several cases we have given the range. The extreme variations were considerable, but not greater than one would expect and not enough to affect the general significance of the findings.

The type of child studied is indicated in the clinical summary of cases appended (Table 1).

The average age of the twenty-one children was 9 months (the range being from 4 to 13 months) and the average weight 5,500 gm. (about 12½ pounds). In general, they would be classed as hospital nutrition cases. Those in Group A, however, were digesting well and gaining satisfactorily in weight; those in Groups B and C were suffering from acute, or more often subacute diarrhea, usually of a non-febrile character. There were no dysenteric cases and none of acute infection or intoxication of the intestines of a severe type.

It will be seen from the table that most of the infants were taking formulas derived from whole milk by various dilutions. This was true in twenty of the thirty-five periods studied. The exact percentages of the milk formulas are given in the table. The numerals indicate the fat, sugar and protein, given in order. Thus, in Case 1, Group A, the food was fat, 2.4 per cent.; sugar, 5 per cent.; protein, 1.8 per cent. The sugar added was lactose unless otherwise specified. In sixteen periods some preparation of maltose was given. Usually this was a fluid preparation, a mixture of maltose and dextrin.

The protein milk (*Eiweissmilch*), which was the food in five periods, was made from whole milk and had the following average composition: Of seven samples, fat 3.00; sugar 2.90; protein 4.00; ash 0.70. It was prepared in 10-quart quantities by precipitating 4 per cent. milk with rennet; the curd was carefully washed twice with water and then rubbed through a fine wire sieve with the addition of 10 pints of special buttermilk (fat-free lactic acid milk) and water added up to 10 quarts.

The high ash content of protein milk shown by the analyses was to us a surprise, since the impression has prevailed that the salts have been much reduced by the removal of the whey and by the washing of the curd. These results, however, were based on seven complete examinations including thirteen samples, some of these being composite samples. Prepared in the manner described, the range of the salts in protein milk was from 0.54 to 0.74 per cent.

TABLE 1.—CLINICAL SUMMARY OF THE CASES STUDIED
GROUP A (STOOLS OF NORMAL CONSISTENCY)

| No. | Name | Age, Months | Weight, Gm. | Food | Period | Dura- tion, Stools Days a Day | Gross Appearance | |
|-----|-------|-----------------|-------------|--|--------|-------------------------------------|------------------|---|
| 1 | P. L. | 10 | 9,600 | 2.4; 5; 2.2. With barley flour | 1 | 3 | 1-2 | Brownish-yellow, largely formed, smooth, firm. |
| 1 | P. L. | 10 | 9,600 | Same as preceding..... | 2 | 3 | 1-2 | Like preceding. |
| 2 | D. W. | 5 | 5,800 | 1.8; 5; 1.6 | 1 | 3 | 4 | Dry, pasty, yellow-brown, not homogeneous. |
| 2 | D. W. | 5 | 5,800 | Same as preceding..... | 2 | 3 | 2 | Like preceding. |
| 3 | W. H. | 12 | 7,000 | 2; 5; 1.8. With cereal gruel | 1 | 3 | 3 | Pasty, gray-green, mostly smooth, partly formed. |
| 3 | W. H. | 12 | 7,100 | Same as preceding..... | 2 | 3 | 2 | Mostly smooth, formed, gray, some softer, greenish. |
| 4 | F. H. | 11 | 4,500 | $\frac{3}{4}$ protein milk; $\frac{1}{4}$ barley water | 1 | 4 | 3-4 | Mostly formed, soft, yellow-gray, smooth. |
| 5 | J. S. | 7 $\frac{1}{2}$ | 4,100 | 1.45; 4.5; 4. Made like protein milk | 1 | 3 | 1-5 | Mostly formed, yellow-gray, smooth. |
| 6 | A. R. | 3 | 5,445 | Protein milk with barley flour | 1 | 3 | 3 | Formed, dry, constipated. |
| 6 | A. R. | 8 $\frac{1}{2}$ | 5,695 | 2.4; 2.6; 2.2. With barley flour | 2 | 3 | 1-2 | Similar, but not so hard. |
| 7 | F. B. | 4 | 5,745 | Protein milk and rice flour | 1 | 3 | 2-4 | Pasty, smooth, largely formed, brownish yellow. |

GROUP B (LOOSE)

| | | | | | | | | |
|---|-------|------------------|-------|---|---|---|-----|--|
| 1 | D. W. | 5 | 5,700 | 1.8; 5; 1.6. With malt..... | 1 | 4 | 5 | Watery, greenish, curds and sour. |
| 2 | J. D. | 5 | 3,900 | 1.6; 2; 1.4. With cane sugar and barley flour | 1 | 4 | 5 | Partly thin, pasty; partly watery, granular, greenish. |
| 3 | V. C. | 4 | 4,400 | 1.8; 2.2; 2. With barley flour | 1 | 3 | 8 | Watery, fine fat curds, sour, greenish-yellow color. |
| 4 | E. R. | 10 | 7,500 | 1.8; 5; 2. With cereal..... | 1 | 3 | 4-5 | Watery, yellow, fat curds, mucus. |
| 4 | E. R. | 10 | 7,400 | Same as preceding..... | 2 | 3 | 5 | Partly watery, partly solid, green, sour, mucus. |
| 4 | E. R. | 10 $\frac{1}{2}$ | 7,300 | 1; 5; 2. With cereal gruel.. | 3 | 4 | 3-4 | Watery, partly green, large curds and mucus, sour. |

| | | | | | | | | | |
|---|-------|-----|-------|--------------------------|--|---|---|-------|--|
| 5 | B. S. | 12 | 8,200 | 2; 5; 18. | With cereal gruel | 1 | 4 | 3 | Watery, gray-green, granular, foul. |
| 6 | W. H. | 13½ | 6,700 | 2; 5; 24. | With cereal gruel | 1 | 3 | 4 | Watery, yellow, fat curds and mucus. |
| 7 | F. H. | 11 | 4,800 | 0; 4; 5; 3.5. | With cane-sugar | 1 | 3 | 11 13 | Orange-yellow, pasty, watery, and much mucus and hard curds. |
| 7 | F. H. | 11 | 4,700 | 1.6; 4.7; 3. | With cane-sugar | 2 | 3 | 8-10 | Watery and pasty, smooth, curds and mucus. |
| 7 | F. H. | 12 | 5,200 | 2; 4.5; 2.6. | With dextrin-tose and sodium phosphate | 3 | 4 | 5-10 | Watery, foamy, fat and hard curds and mucus. |
| 8 | J. G. | 7½ | 4,400 | 2.4; 5; 2.2..... | | 1 | 4 | 4.5 | Watery, fat and hard curds, large fragments. |
| 8 | J. G. | 8 | 4,500 | Same, plus 6 dr. maltose | | 2 | 3 | 4.6 | Watery and soft, spongy, small curds. |
| 8 | J. G. | 8 | 4,000 | Same, plus 9 dr. maltose | | 3 | 3 | 3 | Watery, brownish-yellow, hard curds, foul. |

GROUP C (VERY LOOSE)

| | | | | | | | | | |
|---|-------|----|-------|---|---|---|---|-----|--|
| 1 | B. S. | 12 | 7,700 | 2; 5; 18. | With cereal..... | 1 | 2 | 5-8 | Very watery, green, with fat curds and mucus. |
| 2 | V. C. | 4 | 4,700 | 1.8; 5; 2. | With barley flour | 1 | 4 | 6 | Watery, green, with large fat curds; sour. |
| 2 | V. C. | 4 | 4,500 | 1.8; 2.2; 2. | With barley flour | 2 | 5 | 7 | Like preceding with mucus also. |
| 3 | C. B. | 8 | 4,900 | 2.6; 5; 2.4. | Olive oil 1½ dr.; changed to protein milk | 1 | 5 | 5 | At first pasty with fat curds, then green, very watery, with fat and hard curds and mucus. |
| 4 | F. H. | 10 | 4,500 | 2.6; 5; 2.4 | | 1 | 8 | 11 | Watery, green, foamy, fat curds and mucus. |
| 4 | F. H. | 10 | 4,000 | 2.6; 5; 2.4..... | | 2 | 9 | 9 | Very watery, green, large fat curds and mucus. |
| 5 | W. S. | 5 | 4,000 | 1.6; 5; 1.4..... | | 1 | 2 | 6 | Watery, greenish, little solid matter |
| 5 | W. S. | 5 | 4,000 | Same as preceding, with 8 to 12 c.c. of malted milk | | 2 | 8 | 4.7 | Watery, greenish, little solid matter |
| 5 | W. S. | 5 | 4,400 | Fat-free milk and soy-bean gruel | | 3 | 1 | 7 | Watery, greenish, little solid matter |
| 6 | D. L. | 9 | 5,200 | 1.8; 5; 2.1..... | | 1 | 1 | 10 | Watery, green, with curds and mucus; sour. |

Table 2 gives the percentage of water and dried matter in stools of different types, showing both the averages and the range met with in the series.

TABLE 2.—PERCENTAGE COMPOSITION OF STOOLS STUDIED

| | Stools of Normal Consistency | | Loose | | Very Loose | |
|----------------|----------------------------------|------------|------------------------------------|------------|-----------------------------|------------|
| | Seven Patients Eleven Periods | | Eight Patients Fourteen Periods | | Six Patients Ten Periods | |
| | Average % | Range % | Average % | Range % | Average % | Range % |
| Water | 80.3 | (73-85) | 91 | (88-92) | 93 | (90-96) |
| Dried matter.. | 19.7 | (15-27) | 9 | (8-12) | 7 | (4-10) |

METHODS EMPLOYED

Food and feces were each dried on a steam-bath to a constant weight in equilibrium with room temperature and humidity, and all the determinations were made on this dried material. Each of the urine values was obtained separately from liquid samples. The fat in both the food and the feces was determined by extracting with ether according to a modification of the Soxhlet method and weighing the extract.

Total nitrogen was determined in the dried material and in the urine by the Kjeldahl-Gunning method. We have in our tables regarded all the nitrogen as representing protein; with the knowledge, however, that there is here a small error, as other nitrogen compounds, not protein, are present both in the urine and the stools and possibly also in the food. The amount, however, is so small in the infant as to be negligible for our purposes.

Total ash in dried food and feces and in urine evaporated to dryness was determined in most cases by the Stolte method. According to this method a platinum dish containing the sample is set on pieces of broken pipe-clay inside a porcelain dish. Low heat from a large-sized Teklu burner is applied to the porcelain dish until the material is well charred, after which the heat is gradually increased to the greatest possible point. When most of the black has disappeared the platinum dish is covered by a piece of platinum foil and the heating continued until ashing is completed. No sodium or potassium chlorid is volatilized by this treatment. A few of the earlier samples here reported were ashed over a free flame with the addition of a few drops of acid.

Chlorin was determined in the urine by titration with silver nitrate, according to Volhard. In the dried material in most of the samples the extract, to which nitric acid and ferric alum had been added, was filtered after several hours' standing and titrated with silver nitrate. In the earlier cases the sample was charred, sometimes after being mixed with sodium carbonate, extracted with water, filtered and the filtrate was titrated with silver nitrate.

Phosphates in the urine were determined by titration with uranium acetate or nitrate, potassium ferrocyanid being used as indicator. In the dried material the Neumann method has been used in most cases, that is phosphoric acid precipitated in the ashed material as phosphomolybdate, dissolved by ammonia and reprecipitated by magnesia mixture as magnesium ammonium phosphate and weighed after ignition as pyrophosphate. In some of the earlier samples the Vozárik method was followed. According to this the material is well mixed with magnesium oxid and ashed, the residue dissolved in hydrochloric acid, sodium acetate and acetic acid added to the neutralized solution and phos-

TABLE 3.—TOTAL DAILY EXCRETION

| | Stools of Normal Consistency | | Loose | | Very Loose | |
|-------------------------|----------------------------------|-----------------------------|------------------------------------|--|-----------------------------|-----------------------------|
| | Seven Patients Eleven Periods | | Eight Patients Fourteen Periods | | Six Patients Ten Periods | |
| | Average | Range | Average | Range | Average | Range |
| Water (cc.)..... | 35.6 | (18 - 50) | 133 | (107 - 195) | 293 | (217 - 555) |
| Dried matter (gm.)..... | 8.75 | (6 - 13.1) | 12.95 | (10.43 - 16.76) | 21.16 | (12.6 - 37.35) |
| Fat (total)..... | 3.12 | (0.91 - 7.07) | 4.04 | (0.43 ¹ - 7.35 ²) | 7.97 | (1.39 ³ - 12.95) |
| Neutral fat..... | 1.09 | (0.38 - 2.08) | 2.83 | (0.43 ¹ - 6.48 ²) | 5.70 | (1.37 ³ - 8.24) |
| Free-fatty acids..... | 0.34 | (0 - 2.04) | 0.72 | (0.4 ⁴ - 1.44) | 2.44 | (0 - 7.29) |
| Soap fats..... | 1.69 | (0.46 - 5.40 ⁵) | 0.50 | (0.4 ⁴ - 1.91) | 0.74 | (0.7 ⁶ - 2.17) |
| Protein..... | 2.26 | (1.31 - 3.19) | 3.56 | (2.42 - 5.76) | 5.56 | (3.80 - 10.7) |
| Ash (total)..... | 2.17 | (1.21 - 3.58) | 2.72 | (1.47 - 5.93 ⁷) | 3.96 | (3.03 - 4.78) |
| CaO..... | 1.02 | (0.46 - 1.70) | 1.08 | (0.42 - 2.33) | 0.83 | (0.70 - 0.96) |
| MgO..... | 0.096 | (0.03 - 0.164) | 0.10 | (0.025 - 0.15) | 0.12 | (0.10 - 0.16) |
| P O..... | 0.63 | (0.14 - 1.28) | 0.70 | (0.12 - 1.53) | 0.59 | (0.49 - 0.68) |
| Cl..... | 0.022 | (0.008 - 0.032) | 0.14 | (0.05 - 0.37) | 0.28 | (0.27 - 0.30) |
| K ₂ O..... | 0.180 | (0.084 - 0.300) | 0.36 | (0.22 - 0.52) | 0.82 | (0.68 - 0.97) |
| Na ₂ O..... | 0.041 | (0 - 0.256) | 0.17 | (0.11 - 0.31) | 0.36 | (0.19 - 0.67) |

1. Infant on fat-free milk.

2. Infant on milk containing 1.8 per cent. fat.

3. Infant on fat-free milk.

4. Two infants had none.

5. Very large stools, normal; infant gaining.

6. Six infants had none.

7. Two infants had none.

8. Fat-free milk; intake 9.86.

phoric acid determined by titration with uranium nitrate. Calcium and magnesium, sodium and potassium were determined in dried material of food and feces and urine by the ordinary methods, calcium being precipitated as oxalate and weighed as oxid, magnesium weighed as pyrophosphate, sodium and potassium separated as chlorids and potassium determined by precipitation with platinum chlorid.

Tables 3 and 4 give the actual and the percentage composition of the stools of different types. Very loose stools contain not only a very large amount of water, but the quantity of dried matter lost daily is much greater than that lost in stools of normal consistency. It varies somewhat with the food, but principally with the amount of water.

Fat.—The fats particularly vary in most cases directly with the amount of water. A child who is losing twice as much water is usually losing twice as much fat in his stool. A very high fat loss, however, is also sometimes seen in dry, formed, soapy stools. The average loss of fat in loose stools was two and a half times that seen in normal stools. The percentage of fat varies widely; the average was 37.7 per cent. of the dried matter in the very loose stools, the highest found being 62.2 per cent. of the dried matter of the stool. The highest found in stools of normal consistency was 54 per cent.

The form of fat differs much in the different types of stools. In the normal pasty stools the soap fats are present in largest amount. The soaps form on the average 54.3 per cent., while the neutral fat forms but 39.4 per cent. of the total fat of the stool. In very loose stools these ratios are reversed. The greatest proportion of the fat (64.2 per cent.) is neutral fat, while soaps form but a small proportion (8.3 per cent.) of the total. In eight observations on infants with loose or very loose stools, no soaps at all were formed. This is what might be expected to occur when the intestinal contents are hurried through the bowel too rapidly for saponification to take place. Free fatty acids represent those not combined with bases to form soaps; their amounts also were higher in the loose than in the normal stools and much higher in the very loose stools.

Protein.—The daily amount of protein lost in the stools calculated from the nitrogen is about two and a half times greater in very loose than in normal stools; it being in about the same ratio in the two as the fat. The percentage of the dried matter of the stool which is protein is nearly the same in the stools of the different classes.

Ash.—It is well known that the ash represents a considerable part of the dried matter of the stools, but that in normal, pasty stools it is equal to two-thirds the fat is not generally appreciated. In loose stools about the same relation of fat and ash is preserved, while in watery stools the proportion of fat is relatively higher. The amount of ash in

TABLE 4.—PERCENTAGE COMPOSITION OF DRIED MATTER

| | Stools of Normal Consistency | | Loose | | Very Loose | |
|-------------------------------------|----------------------------------|--------------|------------------------------------|----------|-----------------------------|--------------|
| | Seven Patients Eleven Periods | | Eight Patients Fourteen Periods | | Six Patients Ten Periods | |
| | Average, % | Range, % | Average, % | Range, % | Average, % | Range, % |
| Fat..... | 35.7 | (10.4-81.0) | 31.2 | | 37.7 | (6.6-61.3) |
| Neutral fat..... | | (12.2-66.7) | | | | (17.2-103.) |
| Free-fatty acids.. | 34.9 | (0-65.3) | | 70.4 | | 64.2 |
| Soap fats..... | 10.8 | (14.7-173.) | | 17.7 | | 27.5 |
| Protein..... | 54.3 | (15-36.5) | | 12.3 | | 8.3 |
| | 25.8 | (13.8-40.9) | 27.5 | | 26.3 | (0-27.2) |
| Total ash..... | 24.8 | (13.8-40.9) | 21.0 | | 18.7 | (17.9-50.6) |
| CaO..... | | (13.8-40.9) | | | | (14.3-22.6) |
| MgO..... | 47.0 | | 42.3 | | 27.4 | |
| P ₂ O ₅ | 4.4 | | 4.0 | | 4.0 | |
| Cl..... | 29.1 | | 27.3 | | 19.7 | |
| K ₂ O..... | 1.0 | | 5.6 | | 9.2 | |
| Na ₂ O..... | 8.3 | | 14.2 | | 27.6 | |
| | 1.9 | | 6.6 | | 11.9 | |

some individual cases is interesting. In one normal stool it formed over 40 per cent. of the dried matter of the stool and in one loose stool, over 45 per cent.

When we study the distribution of the salts which make up the total ash it is seen that, while the percentage of the total varies, the actual amount of calcium is nearly the same in normal and loose stools, but is lowest in very loose stools; the quantity of all the other salts, notably sodium and potassium, however, is very greatly increased.

Residue of Dried Matter not Accounted For.—In going over our figures it was evident that there was a considerable percentage of the dried matter not accounted for as fat, protein and ash. This is indicated in Table 5.

TABLE 5.—PERCENTAGE OF DRIED MATTER OF STOOLS NOT ACCOUNTED FOR AS FAT, PROTEIN AND ASH

| Stools | Dried Weight, Gm. | Sum of Fat, Ash and Protein, Gm. | Balance not Accounted for, Gm. | Per cent. of Dried Weight |
|-----------------|-------------------|----------------------------------|--------------------------------|---------------------------|
| Normal | 8.75 | 7.55 | 1.20 | 13.7 |
| Loose | 12.95 | 10.32 | 2.63 | 20.3 |
| Very loose..... | 21.16 | 17.49 | 3.67 | 17.3 |

This unexplained residue varies greatly; in some stools it was only 3 or 4 per cent. of the total; in others it amounted to 25 per cent. of the dried matter of the stool examined. In a review of the literature of the past dozen years we have not found any attempt at explanation of what this unaccounted-for residue is. It is sometimes referred to as "other substances," but usually is entirely ignored.

Exactly what it is has not yet been determined by the direct method. The probabilities are that it is made up chiefly of the cellulose derived from the bodies of bacteria. Evidence of this is found in the carbon content of the dried organic matter after the extraction of the fat. As determined by combustion, the dried matter minus fat was found to contain about 43 per cent. carbon. As protein contains 52 to 54 per cent. of carbon, and carbohydrate but 44 per cent., this substance is probably chiefly carbohydrate. This carbohydrate is certainly not derived from the food. The sugar ingested is either absorbed or undergoes fermentation in the alimentary tract. It is true that many of our children were taking starch, some of them in considerable amounts. But in only exceptional stools could the presence of starch be demonstrated by microchemical tests, and then only in minimal quantities. It was in no case sufficient to account for the carbohydrate content of the stool. Furthermore, just as great carbohydrate content

existed in the stools of many children who were receiving no starch at all. The evidence therefore all points to cellulose derived from the bodies of bacteria as the chief factor in this dried matter unaccounted for.

The proportion of the stool made up of bacteria is great, making, according to various investigators, from 10 to 40 per cent. of the dried matter; in some constipated stools in infants it is estimated to have made up two-thirds of the stool.

TABLE 6.—RATIO OF INTAKE TO EXCRETION AND PERCENTAGE OF INTAKE LOST IN STOOLS

| | Normal | | Loose* | | Very Loose† | |
|-------------------------------------|----------------------------------|------------|------------------------------------|------------|-----------------------------|------------|
| | Seven Patients Eleven Periods | | Eight Patients Fourteen Periods | | Six Patients Ten Periods | |
| Fat | 12.4 | | 23.1 | | 40.5 | |
| Protein | 7.7 | | 14.9 | | 25.2 | |
| Total ash.... | 40.0 | (in urine) | 46.6 | (in urine) | 84.3 | (in urine) |
| CaO | 67.2 | Trace | 70.2‡ | Trace | 79.0 | Trace |
| MgO | 56.7 | Trace | 66.0 | Trace | 100.0 | Trace |
| P ₂ O ₅ | 36.9 | 36.7 | 41.4 | 36.0 | 48.3 | 41.7 |
| Cl | 3.7 | 79.0 | 17.7 | 70.2 | 52.9 | 17.0 |
| K ₂ O..... | 15.4 | 54.9 | 37.9§ | 37.9 | 83.7 | 26.6 |
| Na ₂ O..... | 12.3 | 67.5 | 37.0 | 28.2 | 103.0 | 5.7 |

* In six periods the sodium and potassium distribution was not determined.

† Complete distribution of ash was determined in only four periods.

‡ Fourteen periods.

§ Eight periods.

Ratio of Intake to Excretion.—In the normal stool the loss of fat was but 12.4 per cent. of the intake, while in the very loose stools it reached 40.5 per cent. It is known that fat may be demonstrated in the stool when none is given in the food, it being derived from the intestinal secretions; but the amount is very small and from a nutritive point of view it is a negligible quantity. The loss of protein in the normal stool estimated from the nitrogen content represents but 7.7 per cent. of the intake. This shows how completely the protein of cow's milk is digested and absorbed by the average child. In the loose stools, calculating all the nitrogen as representing protein, the loss is 14.9 per cent. of the intake, and in very loose stools it is 25.2 per cent. This is not strictly true. In loose stools, and especially in watery stools, a considerable amount of protein present is not derived from the food, but is drained away from the body in the intestinal secretions. How much this is we are as yet unable to estimate, but it must be quite large. It is probable that although the infant with diarrhea loses over 40 per cent. of the fat which is given, he does not lose 25 per cent. of the protein given. This is incidental, but very important confirmatory evidence of

the value of protein feeding in diarrhea which has received so much support from clinical observations. When we study the distribution of the salts which make up the ash it is evident that they are not derived entirely from the food ingested, but that they represent a considerable draining away of salts from the body itself. In normal stools nearly four-fifths (76.1 per cent.) of the ash is calcium oxid and phosphoric acid, probably existing in the stool as calcium phosphate, while the proportion of chlorin and potassium and sodium oxids together form but 11.2 per cent. of the total. In the dry, formed stools the ash is often high, due to the bases combined with the fats as soaps.

In very loose stools we found calcium oxid and phosphoric acid to form but 47.1 per cent. of the total, but there was a great increase in the proportion of sodium, of potassium and of chlorin; together they make up 48.7 per cent. of the total ash, the chlorin being nine times, the potassium oxid three and a half times, and the sodium oxid six times the proportion in normal stools. This cannot be without significance.

Normally, 40 per cent. of the ash intake is lost in the stools; this is chiefly calcium phosphate, of which cow's milk has so great an excess. In very loose diarrheal stools there is lost 84.3 per cent. of the intake. The proportion of calcium phosphate shows but a moderate increase over that in normal stools, 79 as compared with 67.2 per cent. of the intake. The great increase in the total is made up of the other salts. The magnesium loss is 100 per cent., indicating that it very slowly enters into combinations in which it can be absorbed. The loss of calcium and magnesium occurs almost exclusively in the stools, only traces being found in the urine. Of the remaining elements, the loss in the urine must be considered in estimating the balances. Chlorin, potassium and sodium are normally present in the stools in relatively small amounts, but in the urine in large amounts. In diarrheal stools we find an enormous increase in the quantity present in the stools and a corresponding reduction in the amount eliminated by the urine. But the increase in the stools is so great as to create a negative balance of 10.3 per cent. in potassium and 8.7 per cent. in sodium. This indicates the loss from the body itself.

The ratio of the loss of salts to the intake is one of the most striking characteristics of loose, diarrheal stools and furnishes an important suggestion as to treatment. In attempting to supply this loss by hypodermoclysis it should be remembered that not only are water and sodium needed, but potassium and magnesium as well. With these facts in mind a better solution for use in hypodermoclysis can certainly be devised than a normal saline or than Ringer's solution.

This subject is still under investigation at the Hospital Laboratories and the foregoing is to be regarded in the nature of a preliminary report.

SOME STUDIES IN FAT INDIGESTION *

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The studies which we are carrying on at the Infants' Hospital in cases of chronic indigestion from fat do not yet include a sufficient number of cases to permit me to present a mass of statistical evidence from which positive conclusions can be drawn. It is difficult to accumulate evidence of final value in a clinical study of this kind. So many cases cannot be investigated as thoroughly as we could wish, and there are so many adventitious circumstances which interfere with the value of our conclusions, that I realize that the evidence they afford is at best but a general impression, not supported by real proof. At present, all I can do is to describe the method which we are employing, and to state the provisional conclusions which we have formed at the present stage of our investigations.

The diagnosis of chronic indigestion from fat is based on the fact that there is evident in these cases a marked intolerance of cow's milk fat. This intolerance shows itself in the inability of the child to take the amount of fat which the majority of artificially fed infants can take, without showing signs either of failure of fat absorption, or disturbance of digestion, or both. In other words, the cases of babies in whom the giving in the food of a moderate amount of fat is followed by the appearance in the stools of free fat or excessive soap, or in whom an increase in the amount of fat given in the food produces immediately symptoms of indigestion and nutritional disturbance, are classified and treated as cases of fat intolerance. In most cases the two conditions of indigestion and deficient fat absorption coexist.

The number of cases of fat indigestion treated in the hospital since it was opened on March 3, has been greater than the number of cases of indigestion from overfeeding, from protein, from carbohydrate, or with fermentation. This does not mean that this is the most frequent form of indigestion seen in infants. The cases received at the Infants' Hospital are, to a large extent, selected cases, chosen from a number of out-patient clinics, and referred to the hospital because they are not doing well. I think it safe to say that a great many of the worst cases come to us. The preponderance of cases showing fat intolerance means

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only that this form of indigestion is the most serious, resistant and difficult to treat. The majority of the patients, when received at the hospital, showed the most extreme degree of malnutrition, being in appearance typical of atrophy, some of them being actually moribund. The number of cases studied was actually no more than thirty-five. This number is so small that it seems hardly worth while to present the results of the studies in statistical form, with tables and figures.

Cases of fat intolerance show a certain constancy in their clinical behavior. This constancy, however, is not found in the clinical symptoms of indigestion, but rather in the manner of their response to attempts to feed them. I mean by this that there is not a constant or typical macroscopic appearance of their dejecta. The movements may or may not look undigested, with soft so-called "fatty curds," or may be white, or brown, or green. They are apt to appear abnormal in some respect, but may not. Vomiting may be absent, or occasionally present, or it may be the only symptom of overfeeding with fat. The typical feature of fat indigestion may be summarized in these words: inability to gain with fat, and inability to gain without it. I mean by this, that if these babies are given a quantity of fat so small that they show no signs of fat intolerance, they lose weight or fail to gain; when more fat is given they show signs of fat intolerance and continue to lose. One peculiarity of these cases we have noted again and again — when the quantity of fat given is increased, in the hope of obtaining a gain in body weight, the babies are apt apparently to respond. They show a gain in weight, and the signs of fat intolerance do not develop at once. Excessive soap, however, appears in the stools, while they are gaining in weight, and then, often after many days, suddenly, within a day or two, they lose all the weight they have accumulated, and more. This phenomenon is so frequent and striking that at the hospital it has come to be commonly called a "blow-up." These "blow-ups" are usually attended by a reappearance of such symptoms as vomiting, bad movements, or even diarrhea. Sometimes they have been accompanied by marked signs of collapse, with cold extremities, cyanosis, and slow pulse. In two of our cases, such "blow-ups" have been fatal.

We have been, and still are, studying these cases by giving various foods, controlling our observations by frequent microchemical examinations of the stools. I realize that such a method of study cannot reach the bottom of the nutritional questions involved, and at best can only give us a clinical basis for procedure. We must look to more complicated studies on metabolism for a final decision.

The points which we have studied are the following:

1. Are there any striking predisposing causes for fat indigestion?

2. Can we successfully compensate for deficient power to digest and absorb fat, by increasing carbohydrate or protein, and if so, to what extent?

3. Is the microchemical examination of the stools for fat a reliable guide to the feeding of these infants, and if so, to what extent?

4. What are the relative values of maltose and lactose as the carbohydrate element in these cases?

5. What are the relative values of precipitated casein and unmodified protein in these cases?

6. What is the value of lactic acid milk in these cases?

The conclusions we have reached have been the following:

1. In looking over our records I have been much struck by the frequency of some evidence of tuberculosis or syphilis in these cases, especially tuberculosis. In two fatal cases tuberculosis was found at necropsy, and in quite a number of others there were some signs, either a tuberculin reaction, signs in the chest or a suspicious radiogram. I am inclined to think that tuberculous babies are especially prone to fat intolerance.

The study of the previous feeding in those cases gave a very unexpected result. In extremely few instances was there any history of overfeeding with fat. In general, the history in these cases is one of overfeeding with carbohydrate. Milk mixtures with excessive sugar, especially cane-sugar, condensed milk, and the various carbohydrate foods, are the usual previous feeding. In a large proportion of cases the previous history suggested carbohydrate indigestion, the clinical features being frequent green irritating movements, vomiting, regurgitation, and much gas and colic.

This finding is interesting in connection with our theories as to the cause of fat intolerance in artificially fed babies. There is some difference of opinion as to whether, in these cases of atrophy, the first injury comes from the nature of cow's milk fat, from the nature of the cow's milk salts, or from excessive carbohydrate fermentation. Our evidence would point to the last of the three. Of course, feeding with various carbohydrate patent foods, or with excessive sugar, is such an extremely common method that the frequency of its general use may account for the frequency of its occurrence in our series. Nevertheless, I am strongly inclined to the view that it is an important cause of failure to digest and absorb fat. These infants after they entered the hospital usually presented an entirely different picture from that described in their histories. They took care of all the carbohydrate we gave them, but they showed this marked intolerance of fat. The effect of long-continued fermentation from overfeeding with

carbohydrate may well be a failure of the power of digesting fat, the carbohydrate injury being primary, but the fat indigestion coming to dominate the picture.

2. In answer to the question as to how far we can compensate for deficient fat digestion by the giving of more carbohydrate and protein, I would say, to a very slight extent. Some cases of fat indigestion, the milder ones, yield readily to proper feeding, and the babies gain weight for a long time with very little fat, or even no fat, in their food. These, however, are babies who seem to have a low caloric requirement; at any rate the quantity of carbohydrate and protein given is not excessive. The majority of the severe cases, such as we get at the hospital, will not gain on moderate quantities of carbohydrate and protein as a substitute for fat. If these quantities are increased, signs of indigestion quickly appear. We have had several cases in which edema and tetany have suddenly appeared, and it is curious that they were all cases on a food relatively high in protein.

3. As to the value of the microchemical examination of the stools, I believe that frequent examinations of the stools for fat are absolutely essential to the proper treatment of these cases. No case of "blow-up" from fat has occurred without the finding of an excess of soaps (and sometimes free fat) in the stools before the occurrence of the upset. The important question, however, is whether the finding of an excess of soap in the stools is a positive indication for reducing the fat in the food. A certain number of babies would not gain in weight until the quantity of fat was increased to such an extent that excessive soap was present in the stools. In some of these the excess of soap lessened and finally disappeared. Others continued to gain until their discharge from the hospital without any lessening in the excess of soaps found. Excess of soap is not incompatible with prolonged gain in weight. On the other hand, in so many cases in which the patients were gaining in weight and showing excessive soap in the stools a "blow-up" did occur, that there is undoubtedly a great risk in continuing to feed the babies so much fat. Moreover, I find that some of the patients that were gaining at the time of discharge with excessive soap in the stools, experienced a "blow-up" subsequently, after quite a long time. Therefore I believe that, in cases in which the patients are gaining, one should make frequent examination of the stools for fat, and if the quantity of soap does not lessen or increases, the fat must be cut down, even if the babies have to undergo a further period of failure to gain, or even of loss in weight. Free fat in the stools should always be a positive indication for cutting down the quantity of fat in the food.

4. The question of the relative value of maltose and lactose as the extra sugar added in cases of fat intolerance was studied as follows:

In cases in which there was intolerance of a definite quantity of fat when lactose was used, a fresh start was made, maltose being used instead as the extra sugar, and the fat was increased in exactly the same way as before. If the babies appeared to be able to gain on maltose, the sugar was changed back to lactose, without any other change, in order that we might see if they became worse. In some cases, when intolerance of a certain quantity of fat developed with lactose, the extra sugar was changed to maltose without reducing the fat, in order that we might see if their tolerance of fat improved.

We have concluded that, in general, cases of fat indigestion do better with maltose than with lactose, and we believe that in the feeding of these patients maltose is the preferable extra sugar. Nevertheless, the evidence is somewhat contradictory. The conclusion supported by the most consistent evidence is that patients with fat intolerance will gain weight and do well on a smaller quantity of fat when maltose is used. A number of patients that would not gain before the fat was increased sufficiently to produce signs of fat intolerance, did gain and do well on a smaller quantity of fat when maltose was used. And in some of these, changing the fat back to lactose caused a failure to gain in weight. No patient did better on lactose than on maltose. There is much less evidence, however, that the use of maltose actually increases the tolerance of fat. It is true that in some cases in which the fat was gradually increased a second time, with maltose in place of lactose, an increased tolerance for fat was found. This occurred, however, no oftener than might be accounted for by a general tendency toward improvement after a period of diminished quantity of fat in the food. In other cases, the fat intolerance developed with the same quantity of fat with maltose as with lactose. Some patients who showed increased tolerance for fat with maltose showed less tolerance when the sugar was changed back to lactose, but this has not occurred often enough to seem very significant.

I believe that the chief value of maltose in these cases is that it is the best carbohydrate to replace the deficiency of fat—to meet the caloric need created by the fat intolerance. The action of maltose in this respect may easily be explained theoretically. Maltose is split during the process of digestion into the two molecules of the monosaccharid dextrose, of which it is composed. Dextrose is probably less fermentable and more easily absorbed than either the galactose of lactose or the levulose of cane-sugar. It has the further merit of being the only carbohydrate which, after absorption, can be immediately utilized for energy production, without undergoing glycogen storing.

It is possible, but by no means evident, that the maltose actually aids the power of digesting and absorbing fat. If this is the case, it

could be explained easily under the theory that sugar indigestion and fermentation is a predisposing cause of fat indigestion. The maltose, being so easily absorbed, leaves behind less fermentable residue, and in consequence, we have less sugar fermentation and better digestion of fat. This, however, is at present only speculative. It would account for the improvement in fat tolerance seen with maltose, but this, as I have said, can also be accounted for by a tendency toward improvement sometimes seen with careful regulation of the amount of fat given in the food.

5. The value of precipitated casein was studied in the same way as maltose by increasing the fat with a definite percentage of unmodified protein, and then with the same percentage of precipitated casein, and by alternating the two forms of protein with the same percentage of fat. Albumin milk was not used; as it is a combination of precipitated casein and lactic acid milk, we believed that its use would not throw so much light on the questions in which we are interested as would the use of its essential elements separately. I am quite ready to admit that albumin milk may be a better food for these infants than any we have tried. But it appears to me to be a sort of shotgun prescription, based on somewhat mixed theoretical conceptions.

The question of the value of precipitated casein is of interest chiefly in connection with the possible rôle of the cow's milk salts in cases of fat intolerance. The essential features of precipitated casein are: first, that its use in place of fat-free milk in modification enables us to diminish the mineral salts without diminishing the protein; second, that it enables us to diminish the lactose to a very small amount, and third, that the casein, being already precipitated in a finely divided form, does not have to undergo precipitation in the stomach. The last feature would not appear to have any direct bearing on the question of fat indigestion, unless there was also protein indigestion. In such a case, more protein might be digested and absorbed with precipitated casein, but we have no evidence pointing toward this. On the contrary, patients that developed signs of protein intolerance with fat-free milk did no better with precipitated casein. The diminution in the lactose with precipitated casein mixtures may be a feature of value, but in view of the effect of changing the extra sugar from lactose to maltose, it does not seem likely that the small quantity of lactose in the fat-free milk is harmful in many cases. If precipitated casein showed a marked superiority in these cases, I should be inclined to attribute it to the diminution in the cow's milk salts.

But it did not show a marked superiority. Here again the evidence is somewhat contradictory. The majority of cases in which precipitated casein was tried did not do better than with the regular form of

protein. Fat "blow-ups" occurred with the same quantity of fat with precipitated casein as with unmodified protein. We have as yet had no case which gave evidence of being able to digest without symptoms more protein with precipitated casein than with total protein. On the other hand, we have had patients who gained better on precipitated casein than on total protein. Some continued to gain when the form of protein was changed back again; others did not gain so well. We have had one case in which the fat tolerance was found increased when precipitated casein was substituted for the usual form of protein, and in which fat intolerance developed when the protein was changed back again.

I cannot conclude that precipitated casein may not be of value in some cases of fat indigestion. In the majority of cases it promises no advantage over the usual protein. Our results have been rather against the rôle of the cow's milk salts in producing fat indigestion, but I believe this to be still an open question, in view of the opposite results which many observers have published.

6. Lactic acid milk has not been sufficiently studied to afford the drawing of even provisional conclusions in fat indigestion. We have not as yet found evidence of its value. We have had cases of protein indigestion develop under its use.

I might give the following summary of the ideas which we now hold at the Infants' Hospital as to the treatment of these severe cases of fat indigestion:

The milk modifications used must be low in fat, average in carbohydrate, comparatively high in protein. The extra sugar should be maltose. A certain number of the milder cases will do well on this treatment. Severe resistant cases are those in which the patients cannot gain on a low quantity of fat and cannot tolerate an increase. A large number of cases are so severe and resistant that they can be saved only by human milk. Breast-milk will save most of these cases, even the severe ones, if used in time. It should always be used in resistant cases, whenever it can be obtained. Even a little breast-milk is of value, and may save a patient that would otherwise be lost. After a period of breast-milk feeding, many cases are found no longer severe and resistant to artificial feeding. If breast-milk cannot be obtained, the feeding is very difficult and the outcome uncertain. Excessive increase of carbohydrate or protein will not help these severe cases, and may do harm; I do not believe that more than 7 per cent. carbohydrate or 3 per cent. protein should be given. Whey mixtures are of no help except sometimes in very young babies who vomit curds; they may do harm. Giving the protein in the form of

precipitated casein may be tried, and may help in some cases. There is not sufficient evidence of its value to indicate its use as a routine.

The only way we have of managing these resistant cases without breast-milk is to keep the fat low, and we must be prepared for a period of loss of body weight which may be prolonged. If they begin to gain when the fat is increased, it is no sign of permanent improvement; they may go to pieces at any time. Frequent examinations of the stools for free fat and excessive soap must be made. In the presence of free fat, or in the continuous or increasing presence of excessive soap, the fat should be reduced, even if the baby is gaining. If a "blow-up" occurs when the fat is increased, the fat in the food should be reduced to zero, and then worked up again, slowly. Frequent "blow-ups" diminish the tolerance for fat. The best hope of eventually obtaining an increase in tolerance of fat sufficient to permit a gain in weight is to avoid overfeeding with fat for a long time, even if much weight is lost.

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A STUDY OF CERTAIN CASES OF INFANTILE DIARRHEA DURING THE SUMMER OF 1914 *

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The problem of the diarrheal disorders of infancy, in spite of a tremendous amount of study, is by no means solved. A great step in advance has been the contribution of Finkelstein, who has described a large group of cases showing them to be caused by abnormal changes of the food within the intestine, his "alimentary intoxication." Abroad, this idea has met favor among many of the foremost pediatricians, and the tendency there seems to be to class almost all diarrheal cases as distinct food disturbances, though some brilliant clinicians such as Czerny refuse to recognize the condition.

In this country, sectional differences in observation prevail. In Chicago and in the middle west one undoubtedly sees in the majority of diarrheal cases the typical types described by Finkelstein. In the east a relatively larger proportion of cases of infectious diarrhea have been reported. The researches of Kendall and his associates in the Boston Floating Hospital show very conclusively that in certain years bacillary dysentery is a frequent type of diarrhea seen in the infants in the hospital.

After reading the studies of Finkelstein and then reading the very antithesis, the work of Kendall, both reporting hundreds of cases, one must conclude that both are right, and that the difference in the views as to the etiology of these disorders is simply due to a difference in the material seen. For instance, Kendall and Smith¹ in 1911 report cases in children of bad diarrhea greatly resembling dysentery, but associated with great numbers of gas bacilli in the stools. As the gas bacillus is injured by lactic acid, the treatment instituted was the feeding of buttermilk. Under this treatment the patients improved markedly. When carbohydrate was fed, as lactose, however, the condition became worse, and when the carbohydrate was removed the patients clinically improved and the stools gradually became normal. Further, since the gas bacillus grows only poorly on protein the fact that Eiweiss-Milch is made up of high protein, lactic acid and low carbohydrate led

* Read before the Congress of Pediatricians of the Middle West held in Chicago, Oct. 29, 1914.

* From the Northwestern Medical School and the Sarah Morris Hospital for Children.

1. Kendall and Smith: Boston Med. and Surg. Jour., clxiv, 307.

Kendall to suggest that perhaps a certain number of the cases classed by Finkelstein as food disturbances, improving under albumin milk therapy, might be cases of gas bacillus infection of the milder type. With these ideas in mind we undertook to study our material at the Sarah Morris Hospital this summer from the point of view not only of food disturbances, but also of infectious diarrheas.

Our cases of severe diarrhea up to September number twenty-two. These cases divide themselves into three groups, each of which is



Chart 1.—J. S.; diarrhea from alimentary disturbances. In this and the following charts the solid line indicates temperature and the broken line indicates weight. Under feeding orders, Br. M. indicates breast-milk; C, cream; D. M., dextri-maltose; E. M., Eiweiss-Milch; M., milk. Under stools, B indicates blood; b, brown; c, curds; g, green; M, mucus; N, normal; S, soft; W, watery.

illustrated by one of the accompanying charts: (1) food disturbances; (2) infectious diarrheas, and (3) parenteral infections. By the latter we mean such cases of diarrhea as occur secondary to infections outside of the intestinal tract as a bronchitis, an otitis media or a coryza.

It was somewhat surprising to find that but two of the twenty-two cases of severe diarrhea could be classified definitely as belonging to the group of food disturbances. These two showed the picture of the alimentary intoxication described so clearly by Finkelstein -- a rise in temperature, a sharp drop in weight, watery, green stools, perhaps even bloody, skin of a pale muddy color, fixed staring eyes, tireless deep breathing, an enlarged liver, leukocytosis and glycosuria.

As an example let us take the case of J. S. (Chart 1) aged 3 months. The child was a "feeder" in the hospital, being on two-thirds milk with 1 ounce cream and 2 per cent. dextri-maltose. When the

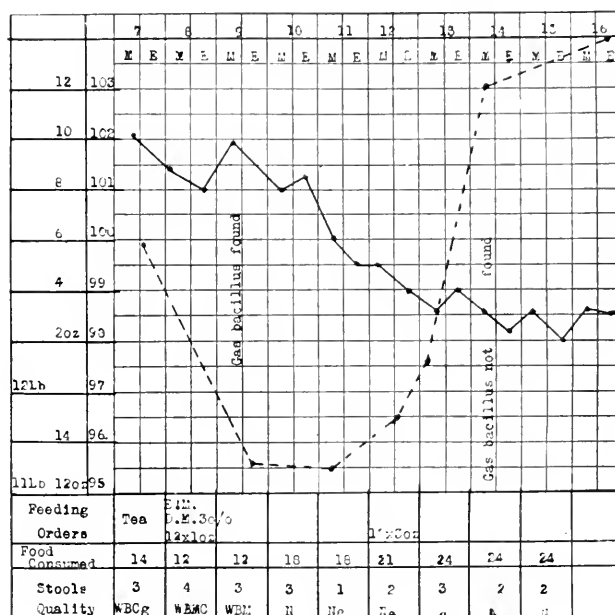


Chart 2.—S. P.; diarrhea with gas bacillus infection.

carbohydrate was increased to 4 per cent. the stools became watery, the child developed a fever, the weight curve dropped and all the above-mentioned symptoms appeared except glycosuria. Physical examination was absolutely negative as regards any foci of infection, and bacteriologic examination of the stools showed no abnormal organisms. Under tea diet for twenty-four hours the acute symptoms disappeared and with small doses of breast-milk the child made a rapid recovery.

In two cases the gas bacillus was found. A typical example is that of S. P. (Chart 2), aged 1 year. He had never been a very strong child, but had had no diarrheal attacks. He was never breast-fed, but received milk, oatmeal water, crackers and cereals. The child had been

ill one week when admitted. The onset was acute, according to the mother, with fever, chilly sensations, headache and diarrhea, six or seven stools per day being passed, soft, green with curds, mucus and blood. He had had a cough for some time and had lost weight since the onset of this attack. Physical examination showed an emaciated child presenting somewhat the appearance of an alimentary intoxication. The mentality was dulled, the respirations rapid and the skin hot, dry and inelastic. Other than this the physical examination was negative, except that the liver was palpable one finger's breadth below the costal margin. Examination of the chart shows that the temperature did not fall on withdrawal of food, that the loss of weight did not cease and that the stools did not at once improve. Finkelstein definitely lays down the law that a fever not disappearing within twenty-four hours or at the very latest forty-eight hours after the withdrawal of food is in the majority of cases not to be considered an alimentary fever. An alimentary intoxication is thus out of the question. Physical examination showed no foci of infection to account for the fever, but bacteriologic examination of the stools revealed the presence of the gas bacillus. Under the treatment instituted, Eiweiss-Milch, the fever slowly came down, the stools improved, the weight curve ascended and the gas bacillus disappeared from the stools. In this case, then, had we not examined the stools bacteriologically we might, after seeing the improvement with Eiweiss-Milch, have classified the case as a food disturbance.

It is striking that the greatest number of our cases were associated with foci of infection in other parts of the body, that is, the parenteral infection group. Whether we were justified or not in concluding that the parenteral infection was the cause of the diarrhea is an open question, but at any rate, the coexistence of the two conditions is certainly worthy of note. This corresponds with the observances of Finkelstein, that is, that the parenteral infections are by all means the most important factor in the production of food disturbances. Of the parenteral infections there were eighteen cases in our group.

A typical example is the case of M. M. (Chart 3) aged 4 months. She had been a healthy baby until the present time and had had no illnesses or diarrheal attacks. The child was breast-fed for two months and also received the bottle, as the mother had to work. For the last two months the child had received 4 ounces of certified milk diluted with an equal volume of water whenever she cried. Four days before admission she was taken acutely ill with fever and diarrhea, she coughed and sneezed, had a temperature of 102 F. and lost some weight. The stools numbered six or seven per day, were soft, green and contained mucus and curds. Physical examination was absolutely

negative as to any organic changes other than that the liver was palpable one and one-half finger's breadth below the costal margin. The child, however, showed the picture of a typical intoxication with dulled, fixed eyes surrounded by deep circles, rapid feeble pulse, very feeble cry, deep respirations, an ashen dry skin and generally toxic appearance. On examination of the chart we find the cardinal symptoms diagnostic of an alimentary intoxication present, the sharp drop in weight associated with fever and bad stools, but we also find the

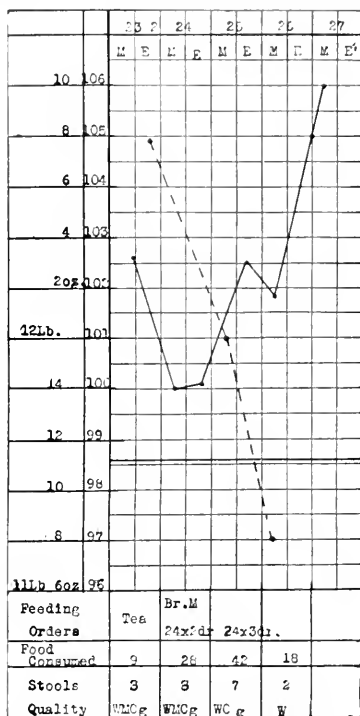


Chart 3.—M. M.; diarrhea associated with parenteral infection (bronchial).

cardinal symptoms of a *primary* food intoxication absent, for on the withdrawal of food for twenty-four hours the temperature does not fall by crisis or the symptoms improve. So in this case alimentary fever is easily ruled out. The cultures from the stools were negative, and, as a definite enteral infection was absent, we must assume that the fever was due to the primary bronchial infection and that the food disturbance was secondary.

Another example is the case of G. H. (Chart 4), aged 7 months. The child was in good health up to the time of admission. She had had no diarrheal attacks before. She was breast-fed for two months and then given a milk mixture of milk, water and sugar. Three weeks

before admission the child was taken ill with diarrhea. This ceased and then a few days before admission commenced again with fever, vomiting and from six to ten watery, green stools per day containing mucus and curds. She lost 2 pounds in weight and has had a chronic cough. Physical examination showed a sickly-looking but not markedly toxic child with rapid pulse and inelastic skin. Dulness was present over the right upper lobe. The chart, as in the previous case, shows first a fever, then a loss of weight and bad stools continuing in spite

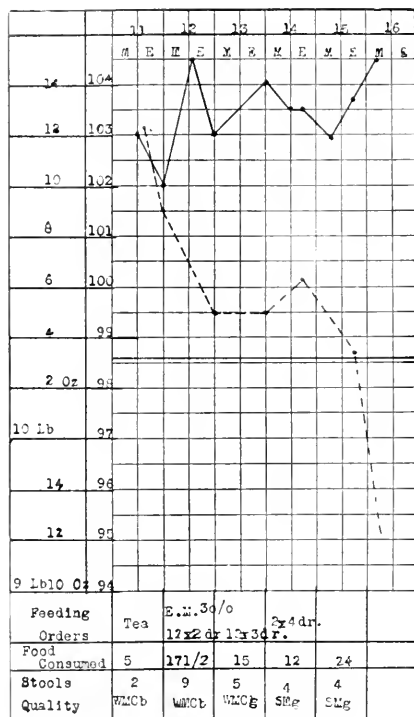


Chart 4.—G. H.; diarrhea secondary to bronchopneumonia.

of the withdrawal of food. Secondly, a careful bacteriologic examination of the stools failed to show any pathogenic organisms. Examination of the patient showed a pneumonia. We must assume, then, in the absence of a primary food disturbance, as shown by the failure of the fever to fall on the withdrawal of food, in the absence of a specific intestinal infection, that the pulmonary infection was the primary disturbance and the diarrhea secondary. The post-mortem examination showed a bronchopneumonia of the upper right lobe and a hypostatic pneumonia of the posterior right lobe. Bacteriologic examination demonstrated the presence of pneumococci in the diseased lung.

In our limited study this summer we have tried to consider every case in the broadest way possible, taking into consideration all of the most important factors in the causation of diarrheal disorders. Studied in this way, out of only twenty-two cases, already three groups emerge, the group of true food disturbances, the group of true intestinal infections and the group of parenteral infections. Why we saw no dysentery is difficult to say. Not a single case studied this summer even clinically resembled the dysentery cases seen in Boston, not even in the nature of the stools, for the gas bacillus cases were not severe enough to be confused clinically with typical dysentery. It is striking that in most clinics abroad and here in the middle West, the diarrheas do not belong to the definite infectious group as they do in the East. In explanation we are tempted to fall back on the work of Brenneman, who settled the great dispute between Europe and America as regards curds in the stools, by showing that *all* observers were correct and that the difference in results was due to the use of boiled milk abroad and raw milk in America. Is it not possible that this difference also explains the discrepancy as regards diarrheal cases? Here in the middle West, we are rather inclined to follow the German teaching and boil our milk. In the East the tendency is to use it raw. The boiling of milk must of course be a great factor in cutting down the number of dysentery cases seen here. That gas bacillus infections occur even with the use of boiled milk is not surprising since the mere boiling, as ordinarily practiced, is not sufficient to destroy the spores of the gas bacillus. In the three groups of cases brought out here, we claim no originality, as these groups have been noticed for some time in the European clinics. We shall be satisfied if we have shown that one must not treat his diarrheal cases too dogmatically, that one must study them broadly, open-mindedly and that above everything else, each patient is a patient to receive individual study and care and treatment.

In conclusion we wish to express our thanks to Drs. Abt, Hess and Lackner, and to our associate, Dr. Jampolis, for the opportunity of studying these cases.

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PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON NOSE AND THROAT WITH REFERENCE TO CHILDREN

THE RELATION OF TONSILS AND ADENOIDS TO THE DEVELOPMENT OF
THE CHILD

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The subject of tonsils and adenoids in children is always interesting to the pediatricist, especially from the point of view of their relation to the mental and physical development of the child, and has received considerable attention during the past year.

In the first place, the tonsillar and adenoid tissues are physiologic structures, and their relation to the mental and physical development in children is of extreme importance. The position of the tonsil is such that, owing to its size and location or the fact that it is imbedded or adherent or pathologically altered, it will interfere with the mechanism of phonation, and therefore in early life bear an important relation to the development of speech, and if diseased it will in turn affect physical development.

These glandular structures are apt to be large in children, so that, at the formative age, in which the child is learning to talk, any abnormality of this structure or any interference with the mechanism of phonation may cause defects of speech, or rather, peculiarities of speech, which will be detrimental to the development of the child.

Children, as well as adults, are very impressionable and extremely sensitive to ridicule, and a child is very quick to notice that it has difficulty in saying certain words correctly, or that it has some defect of speech caused by the presence of the tonsil or adenoid, which gives a peculiar intonation. To the child its own voice is natural, and it is only by comparison with others that it notices the peculiarity. Such peculiarity may lead to so-called backwardness, not that the child has any deficient mental capacity, but that on account of the interference with the mechanism of phonation and the fear of ridicule and of being laughed at by its little playmates or schoolmates, the child would rather admit that it does not know than to use its voice and be the subject of ridicule. Such defects are frequently observed in children from $3\frac{1}{2}$ to 6 or 7 years of age.

The same is equally true of the adenoid structure. We know that children who have a large adenoid growth and who are mouth-breathers, have very poor enunciation. They have lack of nasal reso-

nance and difficulty in enunciating, especially in certain sounds and words. Besides, there is a certain mental hebetude observed in children who have this adenoid growth. There is also a peculiar relation to the mentality of the child suffering from enlargement of this gland. Drs. Harrison Allen and J. Solis Cohen were the first, I believe, to call attention to the intimate relation of this gland structure to the brain and meninges.

The child's mentality may be normal, but it would require more effort to attain development in such a child than in one in whom the adenoid structure does not exist, or in whom it is not obstructive.

The child who has enlarged adenoids frequently shows a backward manner, timidity, lack of confidence and in some instances, on account of the interference with the eustachian tube and middle-ear involvement, feels an uncertainty as to equilibrium, is a little uncertain in his gait and feels at a decided disadvantage. This child is also handicapped by the facts that nasal respiration is interfered with, the respirations are entirely through the mouth, and the physiologic process of aeration does not fully take place. This in itself renders the child below par in its physical condition and handicaps it mentally.

While the defects in speech, which are purely mechanical, are not exactly the same as in the enlarged and imbedded or adherent tonsil, yet the effect on the child is practically the same. The child is unable to recite as the other children do, and notices very quickly the ridicule of its classmates, and besides, I am sorry to say, frequently the impatience of its teachers and also its parents. Some children are discouraged by comparisons.

With the removal of the adenoid tissue early in life and a little training on the part of the parents and teachers, it will be found that the child's capacity is equal to any other, and that the handicap was purely a mechanical one.

Usually the pharyngeal tonsil attracts the general practitioner's or specialist's attention only when it is the site of some pathologic process or when from its physiologic growth it becomes sufficiently large to obstruct nasal respiration and interfere with the development of the nasal and facial bones.

In early infancy the tonsil is rarely affected, but in early childhood it too often causes trouble mechanically and systemically.

The tonsil becomes pathologic only when its presence injures the individual, either locally or generally, not because some one discovers a pair of tonsils in that throat. The submerged tonsil, which may be quite small, is more liable to be doing harm than the fairly large, free tonsil. It is only in the last few years that the tonsil has been judged pathologically otherwise than from its size alone. The tonsil that is

more or less submerged is the one that nearly always is to blame for the infective processes about this region and in the neck, and from the neck to the general system.

A submerged tonsil that extends well up into the velum, diseased or not, may cause interference with the normal function of the eustachian tube, and, indirectly, with the middle ear, producing tubal catarrh, or one of the acute or chronic catarrhal or suppurative inflammations of the middle ear. By pressure alone it will interfere with hearing, even before its presence has caused inflammatory action. The tubal adenoid, that portion which sometimes is found in the eustachian orifice and often overlooked in operation, may be the direct cause in early life of serious ear involvement later.

The imbedded tonsil and the adherent tonsil also affect the child's general physical condition, as we all know, owing to the fact that the crypts and pockets formed behind such tonsils always permit of absorption into the lymphatic system of toxic material from the tonsil, which interferes with the general health and physical condition, and in turn would necessarily create a mental handicap. The child is below par, peevish, fretful and irritable, and lacks the energetic vitality of childhood.

The adenoid gland structure is particularly susceptible to inflammatory action and the slightest inflammatory change in this structure will produce in children marked rise in temperature with all the associated febrile phenomena. Frequently we have to deal with febrile conditions in children in which there is no apparent cause for the symptoms present, and the cause of such temperature, with the accompanying systemic phenomena, could be traced directly to the inflammatory condition of this adenoid structure. In any case in which there is the slightest infection, with inflammatory condition of the adenoid structure, the systemic phenomena are all out of proportion to the local cause; that the gland seems to rapidly absorb any toxic material, and that the temperature suddenly rises before there is any very marked constitutional effect.

Children with adenoid structure are more susceptible to cold and the diseases of childhood than those who do not have it, and the symptoms produced by the cold are aggravated in proportion to the amount of gland structure present.

It is vastly important, then, in many instances, not only from a point of view of physical development, but from a point of view of mental development, that these mechanical interferences with phonation such as an imbedded or enlarged tonsil or the obstructive adenoid, be corrected early in life, before habits are formed and fixed; otherwise the child grown to adult age will go through life handicapped both

mentally and physically. Extreme care should be taken in correcting these defects that the muscular structure of the soft palate and pharyngeal pillars are in no way injured, and thereby prevent the formation of any scar tissue which would involve the mechanism of phonation later in life.

Max Toeplitz¹ gives the results of five hundred examinations of the nose and throat in an institution for delinquent boys. To sum up the results of these 500 examinations, 351 boys were diseased, 106 had enlarged tonsils, 89 enlarged adenoids and 116 were combined cases. Of these, 292 required operation, 23 refused it, 24 were operated on by radical methods.

Because of the apparent large number of operations, it was decided not to touch soft adenoids or small tonsils. As a result, 40 per cent. of the cases treated by the physician during the year 1910 were attributed to the presence of adenoids and tonsils. The operative work was then extended in 1911, and 18.6 per cent. of the cases treated were traceable to the nose and throat.

According to T. F. Harrington, adenoids and tonsils will heal themselves in four out of five cases if the child is given plenty of outdoor air. In view of this, 300 boys were reexamined after a year's stay under the most hygienic conditions. It was found that in only six of these had the tonsils and adenoids disappeared; that four not previously affected were now suffering, the remainder had finally to come to operation. At the end of 1912 the general improvement of the hygienic status was marked, this being directly due to the operative work in 1911.

Arthur M. Corwin² points out that beside the morbid adenoid there is no other affection in childhood that is so common and far-reaching in its malign influence on comeliness, comfort, reliability and individual usefulness. He states that symptomatic hypertrophy of adenoids occurs in from 25 to 35 per cent. of all children between 3 and 10 years of age. It is, however, the direct and remote results of their abnormal presence on mental and moral integrity that he specially deals with. Among four hundred children at Bologna, Bonazzolo found that 141 displayed great lack of the power to concentrate attention, and therefore were backward students. In all but twenty-four of these, adenoids existed, and the twenty-four without them had nasal obstruction from some other cause. These children were neurasthenics. They are duplicated by the thousand in every school community as intellectual dwarfs.

In New York it was found that in a school population of 650,000, 30 per cent. of the children were about two years behind their grades,

1. Toeplitz, Max: *Med. Rec.*, March 14, 1914.

2. Corwin, Arthur M.: *Illinois Med. Jour.*, October, 1914.

and that 90 per cent. of these were delinquent because of removable eye, ear, nose and throat lesions. Cronin found, in New York schools, 150 marked defectives who were very backward in their studies and incorrigible in character; 137 of them had enlarged tonsils and adenoids. These were removed, and in six months the children were reexamined. All were doing well in studies, and their characters had undergone marked improvement.

It has been estimated that 40,000 children annually in Minnesota have adenoids that retard them one year in work.

In the United States 20,000,000 children constitute about 20 per cent. of the entire population. Of these twenty million children it is estimated that 75 per cent. suffer from remediable defect, more or less formidable, six million of them having operable adenoids.

The lack of attention, aprosexia, and lowered power of memory, resulting from typical adenoid obstruction and irritation are responsible for an enormous amount of backward and deviate mental development originating in infancy. The child is unable to apply himself to his prescribed work. Thus handicapped he falls behind his fellows and fails to catch up; he is accounted a dunce; he is punished by his teachers and parents, ridiculed by his mates, and soon finds other matters to take his attention. He grows sullen, apathetic or mischievous, and is considered incorrigible and a nuisance.

From a modern point of view, hypertrophy of the lymphatic ring of the upper air-passages, together with high arched palate, hypertrophy of the thymus with the associated deviation of other structures from the normal are considered among the stigmata of degeneracy and therefore to be referred to the same hereditary or acquired influence that results in hypoplasia in general. Certain it is that the hypoplastic infant is peculiarly afflicted with hyperplasia of the glands in question. The hypoplastic child, fundamentally unstable and still further handicapped by enlarged tonsils and adenoids, with their attendant train of evils, is prone to respond nervously in an exaggerated degree to harmful environmental influences and needs careful study and attention to insure the advancement of which he is in a great number of instances capable.

Corwin emphasizes the fact that a multitude of children with normal brains and normal means for developing them, if denied proper surgical attention, will suffer deterioration of their normal gray matter, and therefore of mental force. And though they may not graduate into criminals or degenerates or public dependents, they will be seriously handicapped all their lives.

THE TONSIL OPERATION IN CHILDREN

T. B. Layton⁴ states that while there is much discussion as to the relative merits of tonsillotomy and tonsillectomy, we have not taken time to determine whether too many operations are performed. While we do not know the function of the tonsillar tissue, we have good reason to believe that it forms an early and important line of resistance to infection. The presence of hypertrophy is not alone sufficient ground for operation, as the proper care of the teeth, training in nasal breathing and the working out of a correct hygiene will frequently obviate the necessity for operation. He feels that the dangers from anesthesia, infection, hemorrhage and traumatism are real and not to be ignored in determining on operation, and that all patients operated on should receive prolonged and thorough aftercare. When the throat condition is part of a general lymphatic hypertrophy little may be expected from operation, and it is wise to operate in no case in which the temperature exceeds 99 F., as in this way one may usually avoid complications incident to beginning infectious diseases. He knows of no operation by which so much good is so easily done in carefully selected cases and urges against indiscriminate operation as a means of needlessly bringing this procedure into disrepute.

Thomas R. French⁵ deplores the indiscriminate enucleation of the tonsils and offers a method for making a differential diagnosis which consists in making an exploratory section of one of the tonsils after the patient has been etherized for operation, and this section is immediately examined in a brightly lighted field under a finely ground loupe, with a magnification of from five to ten diameters. If it is found to be free from disease, the remainder of the gland and the one on the opposite side are both removed down to the capsule; but if the gland is found to be diseased, the tonsils together with their capsules are removed by the Sluder dull dissection method. He thinks that, when a substantial portion of one tonsil is diseased, with few exceptions both tonsils are diseased and require complete enucleation, but that only about 20 per cent. of all enlarged tonsils are diseased and require extracapsular enucleation.

Dr. Bryson Delavan⁵ believes that the tonsil must have some useful function in nature which sometime will be better understood, and that the capsule is a valuable organ which should, if possible, be preserved for the protection and support of the pharyngeal wall and the prevention of cicatricial deformities after the operation. He thinks that such deformities are of common occurrence and are highly detrimental to

4. Layton, T. B.: *Lancet*, London, April 18, 1914.

5. Symposium before Brooklyn Pediatric Society, Oct. 28, 1914. *New York Med. Jour.*, Dec. 5, 1914.

the future welfare of the patient. Not every large tonsil necessarily requires excision.

Henry L. Swain⁵ says that the young, growing and healthy tonsils of children should not be confused with older adult tonsils which he characterizes as being of a retrograding, degenerating, and often diseased type of tissue. The common habit of always completely removing all faucial tonsils from all children whenever they come to operation, as for adenoids, and with no further excuse than that they may make trouble later on, is strongly condemned as being "unscientific, illogical and thoroughly reprehensible." He says that it would be quite as logical to remove all inflamed lymph-nodes from the neck, for the faucial tonsils are to all intents and purposes the exact counterpart of these nodes.

Hubert Arrowsmith⁵ goes further than French and says that of those tonsils which need surgery at all before puberty, 90 per cent. may be satisfactorily dealt with by conservative measures, and only the remaining 10 per cent. may require complete tonsillectomy. He says that tonsillar disease may be induced by infection from other focal points, and that the tonsillar flora may be but surface contaminations and without clinical import. He has for many years favored conservatism in tonsillar surgery and is pleased that pediatricists and internists are gradually beginning to adopt the same view.

G. Hudson Makuen⁵ describes some deformities that have followed tonsillar enucleations and how defects of voice and speech must necessarily follow such procedures. He also describes the so-called capsule of the tonsil, asserting that it is not, strictly speaking, a capsule at all but only that depressed portion of the pharyngobasilar aponeurosis in a recess of which the tonsil develops and to which it gradually becomes attached. This aponeurosis is composed of several layers of thin fascia, and in the young subject an extracapsular tonsillectomy may consist merely in the removal of the tonsil together with a very thin, single layer of fascia, which constitutes its so-called capsule; but in older subjects the layers of fascia have become so firmly united that it is impossible to separate them and a thorough enucleation of the tonsil may result in a kind of window resection of the pharyngobasilar aponeurosis down to the important muscles which it covers, leaving an extensive cavity to be filled in with granulation tissue. A tonsillectomy, therefore, in an adult is a much more extensive and difficult operation than it is in children.

NEW EXPERIMENTAL OBSERVATIONS ON THE FUNCTION OF
THE TONSILS

In the course of a discussion of the numerous suggestions which have been put forth as to the functions of the tonsils, F. Henke⁶ expresses his belief that there has been great exaggeration during recent years on the part of some writers in regard to the frequency with which the tonsils form the portal of entry for many general diseases for whose onset they have been held responsible. The great differences in the statistics of various writers, from 80 per cent. (Faerber), to 1.4 per cent. (Pibram), in the case of articular rheumatism, suggest that much doubt still exists on the matter, and it is still a question whether the acute tonsillitis sometimes observed in association with various diseases is not in reality a secondary localization of an infection which has gained an entrance by some other channel. In order to test the capacity of the tonsils for the absorption of particles from the food, a series of rabbits were fed for a week on food containing large quantities of soot and chinese ink. Subsequent microscopic examination never showed any trace of absorption of these substances by the tonsils, although they were freely taken up by the intestines. The results of Lexer, who fed rabbits on virulent streptococci, and after death of the animals found the organisms present in the tonsil-tissue, do not justify the conclusion which he draws, that the tonsils were the only, or even the chief portal of entry of the infective organisms. The latter were present also in other portions of the pharyngeal mucous membrane, and were in fact more numerous in the periphery of the tonsil, that is, in its capsule, and in the surrounding muscular and glandular tissue, than in the tonsil itself.

Somewhat in opposition to the view that even the normal tonsil is to be regarded as a weak spot through which infection commonly enters is the suggestion that it serves as a defensive mechanism, in virtue of the phagocytic action of the leukocytes which migrate actively to its surface. Brieger, however, showed that the cells which pass out of the tonsil-tissue are in reality lymphocytes, and was forced to postulate a lymph-stream which carried these cells passively to the surface. As Levenstein remarks, proof of such a lymph-stream has been hitherto wanting.

A very different view is that of Schoenemann, who regards the tonsils as submucous lymph-glands, and acute tonsillitis as due to infection reaching the tonsil from the area which it drains. Clinical experience lends much support to this idea, and its correctness has been established as a result of experimental injection of the nasal mucous

6. Henke, F.: *Arch. f. Laryngol.*, 1914, xxviii, Part 2.

membrane carried out by Schoenemann in man, with iodine solution, and by Lenart and Henke in animals and man respectively, with solid particles in suspension. It may therefore be regarded as certain that in man there exists a direct lymphatic communication between the nose and the tonsils. A similar lymphatic communication was proved by Henke to exist between the mucous membrane covering the alveolus of the upper jaw and the tonsil, an observation which he claims to be new. As a result of numerous carefully conducted experiments, he was further able to satisfy himself that there exists a constant lymph current passing from the lining membrane both of the nose and of the gums towards the tonsils, and through it on to its free surface. Such a current must act as a powerful defensive mechanism against the entrance of micro-organisms, and the proof of its existence must dispose of the view that the tonsil is not only a useless organ, but a *locus minoris resistentiae*.

The function of the tonsils is therefore comparable to that of the ordinary lymphatic glands. They serve for the production of white blood corpuscles, and act as a filter for the lymph which passes through them. Foreign bodies, bacteria, etc., may be arrested in the tonsils as in the lymph-glands, and there rendered innocuous. As, however, the tonsils differ from the lymph-glands in having a large surface (much augmented by the presence of crypts) freely exposed in the pharynx, they offer an exceptional opportunity to the organism of freeing itself from foreign substances which have gained entrance to the lymph-stream.

It follows that tonsillitis, occurring either alone or in association with some other disease such as rheumatism or endocarditis, is seldom due to infective material gaining entry through the surface of the tonsil, but the result of a secondary infection conveyed by the lymph-stream, the portal of entry being in most cases somewhere in the nose, the accessory sinuses, or the mucous membrane of the mouth.

This view is in no way incompatible with the well-established fact that severe general infections do take their origin from diseases of the tonsil. In this connection it is necessary to distinguish carefully between healthy and diseased tonsils. When, as a result of marked pathologic changes, the tonsil has come to resemble, as Hopmann says, a "choked filter," it is obvious that it should be regarded as a constant source of danger to the body as a whole.

THE ETIOLOGIC RELATIONSHIP OF THE FAUCIAL TONSILS TO TUBERCULOUS CERVICAL ADENITIS IN CHILDREN

A. Philip Mitchell states that in tuberculous disease of the upper deep cervical glands the faucial tonsils have an importance not hitherto

7. Mitchell, A. Philip: Jour. Laryngol., Rhinol. and Otol., April, 1914.

well enough recognized or understood. The position of the tonsils at the entrance to the digestive tract favors infection more with food than with inspired air, a fact of great consequence in considering the frequency with which cervical glands in children harbor the bovine type of tubercle bacillus. Further, the very direct and short pathway between the tonsils and the tonsillar lymphatic glands explains the frequency with which well-marked tuberculosis of these glands may be secondary to a small focus in a tonsil.

He has investigated the faucial tonsils from sixty-four consecutive cases of children suffering from tuberculous disease of the upper deep cervical glands; twenty-four (37.5 per cent.) of these cases showed histologic evidence of tuberculosis in the tonsils. There are no clinical signs by which the condition can be recognized. In the majority of cases the tonsil retains its normal appearance, is small and frequently receding. Occasionally the tonsil is flat and its surface fissured, or it may be hypertrophied, the external surface showing no ulceration. The chief sites for tuberculous lesions in the tonsil are: (1) surrounding the deeper parts of the crypts, especially the supratonsillar group; (2) immediately under the mucous membrane near the mouths of the crypts; (3) deep in the tonsil, close to the posterior capsule. The lesions may be localized or generalized. Experimental inoculation of guinea-pigs and rabbits with pieces of tonsillar tissue yielded positive results in nineteen cases (30 per cent.), and of these the bovine bacillus was present in twelve cases, and the human in three cases.

Mitchell has also investigated the hypertrophied faucial tonsils removed from ninety children, in whom the cervical glands showed no clinical evidence of tuberculous disease; six (6.5 per cent.) of these hypertrophied tonsils gave histologic evidence of tuberculous disease, while nine (10 per cent.) yielded positive results when inoculated into guinea-pigs. The bovine bacillus was present in three cases, and the human in one case.

In conclusion, he says, primary tuberculous disease of the faucial tonsils occurs much more frequently than previously recognized. Considering the frequency with which the upper deep cervical glands are infected secondarily to tuberculosis of the tonsils, there is absolute need of removal of the tonsils in all cases of tuberculous cervical adenitis. The hypertrophied faucial tonsil is the seat of primary tuberculosis rarely as compared with tonsils from cases of tuberculous cervical adenitis.

ASSOCIATION OF FOLLICULAR TONSILLITIS WITH ACUTE
GASTRIC FEVER

Louis Fischer⁸ says that follicular tonsillitis and acute gastric fever are seen in the infant, as well as in the older child, as a sequence to a deranged stomach, following overfeeding. Loss of appetite, or rather a refusal to eat, will be noted; all symptoms pointing to a gastric derangement will be present, and still the predominating symptom will be the patches or follicles on the tonsils, causing pain on swallowing. Fischer emphasizes that too much importance cannot be placed on the necessity for throat inspection in every child that refuses to eat.

The treatment he advocates is as follows: An alkaline laxative such as a 3- to 5-grain dose of compound jalap powder should be given and repeated every three hours until a thorough evacuation has been produced. During this eliminative treatment water should be given liberally, but no food. Locally for the throat, tincture of iodine diluted with an equal quantity of water should be applied once with the aid of a cotton swab. After the bowels have been thoroughly cleansed, chicken soup, skimmed milk or weak tea may be permitted. Afterward, one or two drops, depending on the age, of tincture of nux vomica may be given before meals.

FATAL CAVERNOUS SINUS THROMBOSIS FOLLOWING TONSILLITIS

H. J. Davis⁹ reports the case of a healthy boy, aged 10, who developed on December 27 a unilateral parenchymatous tonsillitis. His two brothers had previously been laid up in the same house with follicular tonsillitis. This had run its usual course. On January 3 the temperature was 104 F., with rigors, and these continued in spite of all treatment until he died on January 13, the temperature being 107 F. January 5, antistreptococcic serum was injected, and the next day the palate and tonsil were incised. January 7, incision was made in the neck, but no pus was found. January 8, swab was taken from the wound and blood taken from elbow vein; swab was sterile, but after prolonged cultivation *Staphylococcus albus* was found in the blood. January 9, the diagnosis of cavernous sinus thrombosis was obvious. The eyelids were edematous and tightly closed over the eye, which was bulging; there was ecchymosis of the conjunctiva, and edema had spread to the forehead and face from blocking of the facial vein and extended down the neck. There was little to be seen in the throat except that the left tonsil was red and slightly enlarged. Incisions were made in the palate, face, neck and eyelids, and the conjunctiva was also incised and 5 minims of liq. ammon. fort. administered every

8. Fischer, Louis: Med. Rec., Nov. 21, 1914.

9. Davis, H. J.: Jour. Laryngol., Rhinol. and Otol., January, 1914.

two hours in water. January 10, twitchings and paresis of the leg supervened; lumbar puncture fluid clear; 4 c.c. drawn off apparently not under pressure. Fluid sterile and did not reduce Fehling's solution. Child died on January 13.

Davis believes that the infection of the cavernous sinus travelled through the facial vein, as it communicates by the angular vein with the ophthalmic vein in the orbit. The edema of the face was due to blocking of the facial vein.

KOPLIK'S SPOTS OCCURRING ON THE TONSILS OF A CHILD

Sydney R. Miller¹⁰ reports the case of a child of 10 months who was suddenly seized with a laryngeal spasm, associated with a temperature of 104.5. Examination of the throat showed a dusky red mucosa with very large swollen tonsils on which were a number of small bluish, semitransparent, elevated bodies, less than pin-head size. These were diagnosed as Koplik's spots which, from a search of the literature, had never been seen in this location before.

The child recovered from the laryngeal spasm after being given a hot foot-bath and was relieved in every way. Within a short time the entire body was covered with a dusky red mottling, characteristic of measles.

Within two days after the appearance of the external rash, the tonsils subsided to normal and no spots could be seen.

Another interesting phenomenon in connection with this case was the discovery that the child was anaphylactic to egg-albumin, which gave rise to laryngeal stridor, fever to 103, an urticarial rash and a swelling of the tonsils. The symptoms came on within a half hour after feeding the child egg-white. A dilution of one drop of egg-albumin in a quart of water was tolerated. The strength was gradually increased until in about three months the child had become desensitized to such an extent that it can now be given one dram of pure egg-albumin without any trouble.

THE EPIPHARYNX IN CHILDREN

According to Edgar M. Holmes,¹¹ over 90 per cent. of all pathologic conditions met with in otology are due to some preexisting pathologic condition in the epipharynx or eustachian tube. He believes that by improved methods in treatment in this locality more and more ears can be saved. Many children affected with middle-ear disease may be entirely relieved by simply removing their adenoids, but it is also well known that many more are but temporarily relieved and then become as bad as before.

10. Miller, Sydney, R.: Bull. Johns Hopkins Hosp., March, 1914.

11. Holmes, Edgar M.: Ann. Otol., Rhinol. and Laryngol., March, 1914.

Were it not for cicatrices and their effect on the eustachian tube the subject of adenoids would be very simple. A large number of the children referred to the specialist by school inspectors do not need an operation and are far better off without one. If an operation has been done, these children should be seen and examined a few weeks afterward with especial reference to adhesions about the eustachian tubes. Holmes' nasopharyngoscope has been of great help in making a good satisfactory examination of the epipharynx.

The treatment is general and local. Gastro-intestinal conditions must be looked after; malnutrition and anemia, and each child's resistance should receive attention. Infections of the epipharynx are almost always associated with those of the nasal cavities. He advises against the douche and prefers medication by means of a dropper. A 10 to 20 per cent. solution of argyrol dropped through the nose has given satisfaction. The solution can be made to run into the ear or eustachian tube by properly tilting the head when held over a table in Rose's position. The removal of bands of adhesion about the eustachian tubes is done by means of special ring curets, the use of which requires some practice.

CICATRICAL PHARYNGEAL DIAPHRAGM FOLLOWING SCARLET FEVER

J. F. O'Malley¹² reports the case of a boy, aged 5, who had scarlatina two years ago, and was then for about three months in a fever hospital. On returning from the hospital it was noticed that he "spoke through his nose," and the condition has become worse since then. He can swallow solids and liquids without difficulty, and there is no history of interference with breathing.

On examination of the throat one sees a diaphragm, appearing as a continuation downwards of the soft palate and formed by the union of the free edges of the two posterior pillars. It shuts off the nasopharynx from the oro- and hypopharynx and is complete except at the center of its upper and lower borders. The upper opening is a small space surrounding the normal uvula, in which the latter is free to move. At the lower border there are two openings, one on each side of a central adhesion, which passes obliquely downward and backward to the right and is attached to the posterior wall of the pharynx, opposite the level of the epiglottis. The anterior pillars, at their upper ends, blend with the new diaphragm, whilst the lower ends are normal and behind the latter. On the anterior aspect of the new formation the tonsils can be seen appearing rather superficial owing to the partial obliteration of the sinus tonsillaris.

12. O'Malley, J. F.: *Jour. Laryngol., Rhinol. and Otol.*, August, 1914.

O'Malley describes the method of formation of these adhesions as follows: There was an intense inflammation with inflammatory infiltration, and at the same time a myositis which put the muscular tissue in a condition of paresis. The swelling and infiltration, especially in the young child, facilitated the coming together of the parts, and the intensity of the myositis prevented the mobility which would otherwise exist and enable the parts to come away from each other. A denudation of the epithelium proceeded at the same time, owing to the severity of the inflammation, and that facilitated the joining up.

TUMOR OF THE SOFT PALATE CONSISTING MAINLY OF SALIVARY
GLAND TISSUE

Thomas Guthrie¹³ reports the case of a boy, aged 8 years, with a pear-shaped tumor hanging from the right side of the soft palate. The tumor was covered with normal mucous membrane similar to that of the surrounding parts, and showed no signs of ulceration. When cut through the middle, after removal, the tumor measured 9 mm. longitudinally and 6 mm. transversely, and was found to consist of a mixed salivary gland of the submaxillary type. Guthrie had not been able to discover any record of a similar case.

DOUBLE ABDUCTOR PARALYSIS IN A CHILD, AGED EIGHT

C. W. M. Hope¹⁴ reports the case of a child, aged 8, who was admitted to the hospital, 1913, with marked dyspnea. Up to fourteen days before admission was perfectly well; gradual onset of dyspnea, but voice was not noticed to be altered.

When first seen the voice was good, but there was marked dyspnea, sucking in of intercostal spaces and supra-clavicular regions; marked retraction of lower end of sternum, and slight cyanosis. Temperature was normal; pulse 120. On examination by the direct method under chloroform both cords were found fully adducted, normal in color, and no movement seen, either of them or of the arytenoids, which were of normal size. There was only a small area for aeration at posterior end of glottis. Intubation was tried with O'Dwyer's tubes, but they were coughed out within a few minutes of introduction. Tracheotomy was then performed. After four days tube was blocked by day and opened by night. Swab from larynx showed absence of Klebs-Loeffler bacilli.

Three weeks later cords showed some movement; there was slight abduction and also some movement of the arytenoids. Tracheotomy tube had been removed and left out on Jan. 14, 1914, but owing to night stridor was replaced (low tracheotomy) on Jan. 29, 1914. Skia-

13. Guthrie, Thomas: Jour. Laryngol., Rhinol. and Otol., February, 1914.

14. Hope, C. W. M.: Jour. Laryngol., Rhinol. and Otol., August, 1914.

gram of chest showed no enlargement of thymus gland or any increase in size of bronchial glands. The cause of the paralysis could not be determined.

SUSPENSION LARYNGOSCOPY IN CHILDREN

Albrecht¹⁵ states that suspension laryngoscopy in children is much simpler than in adults. The reasons for this he ascribes partly to the upright position of the epiglottis, which often permits a satisfactory view as soon as the base of the tongue is pressed on, and partly to the slender build of the neck characteristic of childhood. He states that clinically the procedure has rendered more certain: (1) the removal of the larger infantile nodes ("screamer's nodes") analogous to the singer's nodes in adult life, and ascribed to habitual crying or screaming; (2) the operative treatment of laryngeal tuberculosis; (3) the operative treatment of papilloma, which he considers the great field, and of which he mentions nine cases thus treated. To these three procedures he adds a fourth, enucleation of the tonsils, stating that in operating under narcosis, and with the head dependent, suspension gives a good view of the tonsillar region, so that enucleation can be effected in a few minutes under the strictest visual control.

A CASE OF RECURRING LARYNGEAL POLYPI WITH TETANY

R. Bishop Canfield¹⁶ reports the case of a child 2 years and 3 months old who had been growing more and more hoarse for six months prior to August, 1912, and for the past ten days had been showing a marked degree of dyspnea; cyanosis had been present for several hours, so that the respiration was gasping. A high tracheotomy was done and immediate relief obtained.

Nine months later the child was seen for the second time. He had been wearing the tube constantly and it had not been even removed for cleaning. The wound was in bad condition. Attempted removal brought on a brisk hemorrhage. This was stopped and two days later a bronchoscopic examination was made which revealed a mass of papillomatous tissue filling the larynx and extending down to the level of the lower end of the tracheotomy tube. This mass of tissue was removed and applications of absolute alcohol made; the tube was replaced. Two months later, the condition having not improved, a thyrotomy was performed and the growth thoroughly removed under ether. It was found to extend up onto the base of the tongue.

Ten days later the tracheotomy tube was removed, but had to be replaced and was worn for two months longer. At this time the larynx was intubated and the tube taken out of the trachea.

15. Albrecht: *Jour. Laryngol., Rhinol. and Otol.*, February, 1914.

16. Canfield, R. Bishop: *Ann. Otol., Rhinol. and Laryngol.*, March, 1914.

Dec. 13, 1913, the intubation tube was removed under suspension laryngoscopy, but edema quickly came on because of relief of pressure and the tube was reinserted. The edema became so great, however, as to cover the top of the tube, and it was necessary to replace the tracheotomy tube again.

Five hours afterward the child complained of being cold and developed a tremor resembling a chill; the temperature rose to 103.8 F., respirations 28 to 40 and pulse 80. There was profuse sweating. Within two hours the tremor had developed into clonic convulsions, beginning in the face, then the arms, hands and fingers, and lastly the legs. The convulsions became almost continuous and lasted several hours; the child became stuporous; opisthotonus appeared; erythematous rash developed over the chest and face. Three days after the first tremor the convulsions became tetanic and from then on the case was plainly one of tetany. The attack lasted thirteen days, during which optic neuritis developed from edema and the child was blind. After this the child gradually improved, vision returned and is good, and the child still wears the tracheotomy tube.

The cause of the tetany was believed to be either a toxemia from ether or an injury to the parathyroid from hemorrhage during some of the operative manipulations.

SINUS SUPPURATION IN CHILDREN

Suppuration of the accessory sinuses is more common in children than is generally supposed and the following cases reported by Dan McKenzie¹⁷ are very interesting.

CASE 1.—Frontal sinusitis in a girl aged 7. There was a curious history in the case. About three months before she came to the hospital patient was overturned by a bicycle and thrown on her face. A fortnight later pain and swelling in the left supra-orbital region and around the left eye set in, together with headache and pyrexia. After about ten days of fever and headache, the patient being confined to bed, a sudden gush of pus from the left nostril took place. Thereupon the pain ceased, the fever left her, and the child was able to be up and about; but the discharge from the nose continued. When she came to the hospital pus was seen to be oozing freely from under the left middle turbinal. A skiagram showed well-marked frontal sinuses on both sides, and the left frontal sinus together with the left antrum threw shadows. Treatment was confined to nasal drainage; the left middle turbinal was removed and nasal antrotomy performed, and the discharge gradually ceased.

CASE 2.—Double maxillary antrum suppuration in a girl, aged 12. After washing out the cavity several times with a Lichtwitz trocar, the radical antrum operation was performed on the left side and simple nasal antrotomy on the right. The discharge has now ceased.

CASE 3.—Left frontal sinusitis in a girl aged 15; radical Killian operation; necrosis of the bridge. The patient is now aged 17, her operation having been performed two years ago. The case was one of ethmoidal suppuration with polypi. After curetting and drainage the presence of headache and local pain

17. McKenzie, Dan: *Jour. Laryngol., Rhinol. and Otol.*, April, 1914.

led to the radical frontal sinus operation (Killian). The bridge necrosed and was removed a fortnight later, but the wound had healed with very little deformity on account of the natural flatness of the patient's nose. There was still a fair amount of discharge.

ORBITAL ABSCESS WITH OPTIC NEURITIS DUE TO ACUTE ETHMOIDITIS
IN A CHILD

J. H. Guntzer¹⁸ reports the case of a girl, aged 7 years, a normal child and in apparent good health, who came to the hospital on March 18, 1914. She had had no recent illness until the right eye became swollen two days before.

There was well-marked orbital cellulitis, the upper and lower lid swollen with tenderness over the inner margin of the orbit, marked exophthalmos with displacement of the eyeball downward and outward, ocular motion limited above and internally, the eye dilated outward. Diplopia; vision 20/200. Conjunctival blood vessels injected. Fundus examination showed the veins enlarged, tortuous, the arteries normal. Disk-color red; margin blurred. Diagnosis: Optic neuritis.

The orbital abscess was incised at the most prominent portion on the nasal side below the brow in order to relieve the ocular pressure. The following day the ethmoidal labyrinth was exenterated by the external route. The patient made an uninterrupted recovery. Six weeks after operation the eye-ground had entirely cleared up with vision 20/20.

1517 Walnut Street.

18. Guntzer, J. H.: *Laryngoscope*, September, 1914.

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THE INFLUENCE OF POSTURE ON DIGESTION IN INFANCY *

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Success in infant-feeding depends not only on the composition of the food, but also on the way in which it is given. The manner of feeding and the management of the child between feedings have received scant attention, yet there are certain points of considerable importance in this connection disregard of which may result in unsuccessful feeding, no matter how carefully the food is prescribed.

Posture has an important bearing on digestion in infancy. For many years the teaching of doctors and nurses has been that an infant must be put to sleep in the horizontal position immediately after feeding. Many mothers, however, hold the child upright after feeding before putting him down to sleep. It is believed that one of these plans is correct and the other wrong, both in theory and practice, and that the Roentgen ray has demonstrated the truth of this. The way in which posture can affect digestion depends on two main factors.

The first factor concerns the anatomy of the stomach. Roentgenography has shown the fallacy of the old idea that the stomach in infancy is vertical in position. There are several "types" of stomach which resemble the adult types in a general way, but the shape of the stomach depends on the amount of food and gas present, pressure from the outside, posture, etc. These different types have no especial importance. There are certain anatomic features which have to be borne in mind. The esophagus enters the abdomen by an opening in the diaphragm, almost in the mid-line, in contact with the aorta and the ventral surface of the bodies of the vertebrae. The cardiac orifice lies just to the left of this position and the cardia is held firmly to the posterior abdominal wall by the esophagus as it pierces the diaphragm. The fundus of the stomach lies in the left paravertebral groove, that is,

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* Presented in part at the Pediatric Section, N. Y. Academy of Medicine, April, 1914. From the Pediatric Division and Roentgen-Ray Laboratory, St. Luke's Hospital.

in the lateral recess formed by the projection forward of the vertebral column into the abdominal cavity. The fundus reaches a plane considerably dorsal to the cardiac orifice. It is covered in front only by the liver and extends to the anterior abdominal wall. The pyloric end of the stomach is pushed forward by the vertebral column, pancreas and duodenum. The pyloric opening is directed backward toward the duodenum, but lies in a plane which is ventral to that of the cardia. The cardiac opening is behind the center of the anteroposterior diameter of the stomach.

The second factor is that there is a certain amount of gas in the stomach of every individual. This is a matter of common knowledge, but has been emphasized by the Roentgen ray. Practically every roentgenogram taken in the erect position shows a bubble of gas in the fundus end of the stomach (*Magenblase*). In the prone position it is not possible to estimate accurately the amount of gas present, as will be shown later. This gas may be derived from three sources, namely, swallowed air, gastric fermentation and intestinal gas.

Gastric fermentation is rare and is an important source only when there is stagnation from obstructed pylorus or from gastric atony of extreme degree. Intestinal gas does not commonly pass back into the stomach in all probability. Swallowed air accounts for the gas in the stomach in the large majority of cases. Air-swallowing takes place constantly, though to a variable degree. The size of the pharynx is such that it is rarely filled completely with food at the time of each swallowing act, and its anatomic relations prevent its collapse on a small amount of fluid. Air is constantly present in the pharynx and some air is forced down with the food by the contraction of the swallowing muscles. It is often possible to hear a child gulp down air with each swallow of milk. More or less air may be swallowed with saliva or nasal or bronchial mucus between feedings. Tongue-suckers, thumb-suckers and babies with a "comforter" habit suck and swallow air a considerable part of their waking hours. Infants fed on liquids swallow more air than older children fed on solids or semisolids. The more solid food is swallowed in a bolus and more completely fills the pharynx, while liquids are swallowed a few drops at a time. The smaller amount of air swallowed with semisolids may possibly be the explanation of the cessation of vomiting in the refractory cases in which no liquids are retained, but semisolid porridge is retained.

Usener,¹ in a paper on *Acrophagic*, noted the air-bubble in older children to be smaller than in infants. He stated also that the gas in the stomach has been proved to contain only oxygen, nitrogen and carbon dioxide or merely the constituents of air. He explained the mechanism

1. Usener: *Ztschr. f. Kinderh.*, 1912, v. 440.

of the comparatively large amount of air swallowed by infants as follows: The horizontal position is probably one cause of air-swallowing, as it is in adults in bed with acute illness or after operations who often have great difficulty in swallowing properly and often swallow air with liquids. In nurslings each small drop of milk on reaching the region where the swallowing reflex is initiated starts the reflex and causes swallowing of air with the milk.

Flesch and Peteri,² with the fluoroscope, saw an air-bubble appear with the first swallow and fill one-third to one-fourth of the stomach during the feeding in both breast-fed and bottle-fed infants.

Grulee³ thinks that the gas mostly comes from gastric fermentation due to stagnation from short-interval feeding. If this were true, the air-bubble should be absent when children are fed at long intervals. In our observations such children however, show gas-bubbles but little smaller than those fed too often. The character of the eructated gas suggests fermentation only in cases of extreme gastric stagnation.

Figures 1, 2 and 3 demonstrate the source of the gas in the stomach. This infant was given her usual bottle with bismuth 1:8. She took the first half ounce in about two minutes. Three minutes later the first exposure was made (Fig. 1). It shows a lateral view of the child held in the horizontal position. There is a small amount of milk in the stomach with a moderate bubble of gas between it and the anterior abdominal wall. The child was held in the horizontal position and then given 1½ ounces more of the food in three minutes. Figure 2, taken at ten minutes from the beginning of the feeding, shows a very large amount of gas above (ventral to) the milk. The stomach is greatly distended already. The child was crying and was uncomfortable even with half of the feeding in the stomach. The child was then given 1½ ounces more, but this was taken badly and the last half ounce of the feeding was absolutely refused. About fifteen minutes were spent in trying to get the food down; different nipples were tried, but the child could swallow no more. Figure 3—eighteen minutes after Figure 2—shows why the last half ounce was refused. The enormous gas-bubble plus the milk had so distended the stomach that no more could be taken. This gas must have been swallowed air, since it has appeared during the feeding, there was no stagnation of food from the last meal, and the gas appeared too rapidly to be the result of fermentation. The food contained no substance which could form gas with the gastric juice in amount large enough to distend the stomach to this extent. The bismuth subcarbonate used does not evolve gas

2. Flesch and Peteri: *Ztschr. f. Kinderh.*, 1911, p. 227.

3. Grulee: *Infant Feeding*, Saunders, 1914.

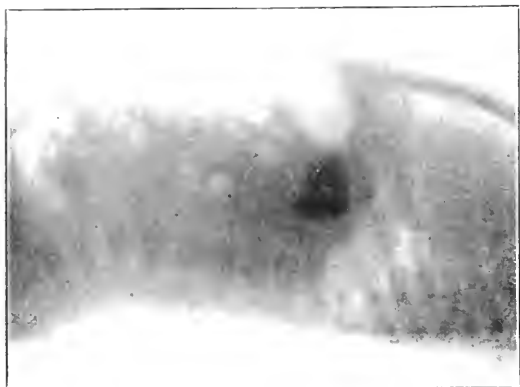


Figure 1

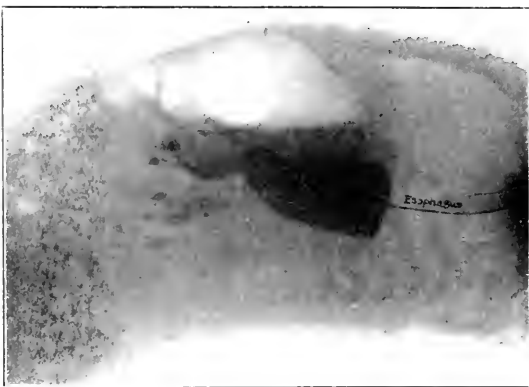


Figure 2

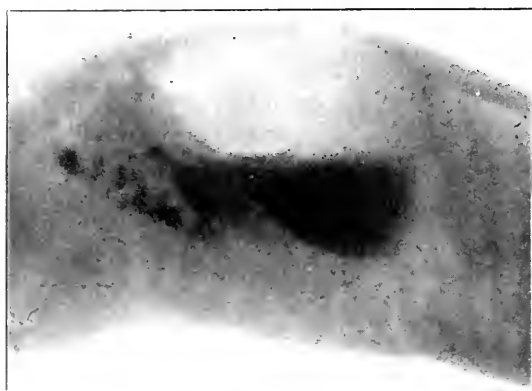


Figure 3



Figure 4



Figure 5

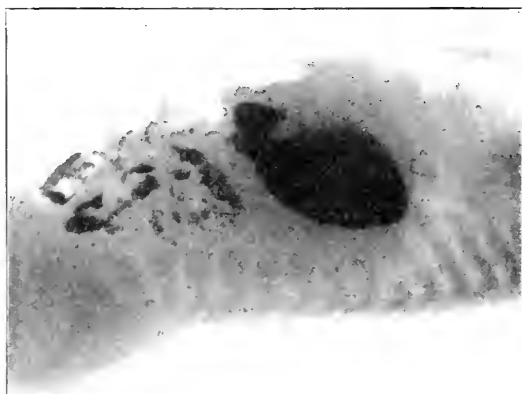


Figure 6

Figure 1.—Child, aged 4 months; shown also in Figures 2, 3, 4, 5 and 6. History of vomiting since birth, on breast and bottle. Nursed eight weeks. Given usual feeding, that is, fat 2 per cent., lactose 6 per cent., protein 1.75 per cent. Four ounces every three hours, six feedings a day. To this $\frac{1}{2}$ ounce of bismuth subcarbonate was added. One-half ounce was taken in the first two minutes. Plate taken five minutes after feeding was begun. Supine position, left side against the plate. There is a small amount of milk in the stomach, with a small bubble of gas anterior to it. There is much gas in the small intestine.

Fig. 2.—The child was then given $1\frac{1}{2}$ ounces more food in three minutes. Plate taken ten minutes after feeding was begun. Supine position, left side against the plate. There is a large air bubble in front of the milk, which has gravitated to the back part of the stomach. A little bismuth has entered the small intestine. Note the position of the esophagus.

Fig. 3.—The child was then given $1\frac{1}{2}$ ounces more of the feeding. This was taken with difficulty, and the remaining $\frac{1}{2}$ ounce was refused. Child seemed in pain, cried and regurgitated a small amount. Plate made twenty-eight minutes after feeding was begun. Position same as above. Enormous bubble of air distending stomach. Note double pouch of fundus and pyloric end of stomach (as in cases of dilatation) in both Figures 2 and 3.

Fig. 4.—Thirty minutes after feeding was begun. Erect position, abdomen against the plate. Milk has gravitated to the lower part of the stomach, forcing air to the upper part. After this plate there was a large eructation of gas. The child at once stopped crying and went to sleep.

Fig. 5.—Thirty-five minutes after feeding was begun. Position same as in Figure 4. Air bubble has disappeared. Note migration of pylorus toward left, as compared with Figure 4.

Fig. 6.—Thirty-seven minutes after feeding was begun. Supine position, left side against plate. The stomach has contracted on the food; little or no gas remains. There is one inch difference in the anteroposterior diameter of the abdomen in Figures 3 and 6. A good deal of bismuth has entered the small intestine. The double pouch appearance seen in Figure 3 is gone.

with hydrochloric acid under 0.5 per cent. This gas-bubble must be composed largely if not entirely of swallowed air.

Food taken by a child enters the stomach and gravitates to its lowest part, displacing the gas present to the highest part. The behavior of liquid and gas in the stomach does not differ from that of liquid and gas in a glass bottle or any other receptacle. When the child is held in a horizontal position the liquid food therefore gravitates to the posterior part of the stomach, that is, the fundus end, and forces the gas present to the anterior part of the fundus and to the right end of the stomach. Since the cardiac orifice is situated well back against the vertebral column, it follows that it will be covered by the liquid and that the gas cannot escape into the esophagus. It can escape only through the pylorus, if at all. If the amount of food plus gas is enough to distend the stomach, either food and gas must be forced out through the pylorus, or regurgitation of food must take place through the esophagus until the tension on the stomach wall is relieved. The horizontal position causes a perfect water-lock to form as far as the gas and the cardiac opening are concerned. This may be readily imitated by taking a bottle two-thirds full of liquid. When the bottle is held on its side no air can escape through the bottle mouth. When the bottle is held upright, the gas can escape with ease if under pressure.

When a child is held upright the liquid gravitates at once to the dependent part of the stomach displacing the gas to the highest part — that is, to the upper part of the fundus — and this makes it possible for the gas to escape by the esophagus. This often takes place at once as soon as the child is held erect.

Figures 3 to 6 show the effect of posture. Figure 3, as stated above, shows the enormous distention of the stomach with gas in the horizontal position. Two minutes later the child was held upright and Figure 4 shows the milk at the lower, the gas at the upper part of the stomach. The child was then held against the mother's shoulder, patted gently on the back and at once eructated a large amount of gas. He then became perfectly quiet, stopped crying and dozed. Figure 5 — five minutes later — shows that the gas has been almost entirely eructated and that the stomach has contracted on the food. Figure 6 — two minutes later — shows again a lateral view, in the supine position. There is only a small bubble of gas against the anterior abdominal wall. The rest of the stomach has contracted on the food. The pyloric end shows well and there is a good deal of bismuth in the intestines. The comparison between Figures 3 and 6 is most instructive, and corresponded to the physical signs in the epigastrium and to the child's comfort. To one seeing only the picture shown in Figure 6 it would not seem possible that the same stomach could hold the amount of gas shown in Figure 3.

Figures 7, 8, 9 and 10 also demonstrate what happens when an infant is fed in the ordinary horizontal position and is allowed to remain in that position. This child was a normal healthy child of 6 months in the hospital while his mother was undergoing an operation. He was given his usual bottle with one-half an ounce of bismuth subcarbonate, which he took readily and easily. During the feeding he was kept in the horizontal position. His abdomen, which was moderately distended before feeding, became much more so during the feeding and the child showed every sign of acute discomfort. He began to cry, squirmed as if in pain and at the time of the first exposure, three minutes after feeding, began to regurgitate milk. This took place easily without any violent vomiting effort.

The Roentgen ray shows the reason for these phenomena. Figure 7 shows a lateral view of the abdomen in the supine position. The milk in the stomach has gravitated into the posterior part and has displaced the gas to the anterior part of the stomach. The esophagus shows plainly as the child was regurgitating during the exposure. Its position well below the level of the milk shows plainly. It is perfectly evident that no gas can possibly escape from the esophagus until enough milk has been vomited to uncover the cardiac orifice of the stomach.

The child was then held erect and the second exposure two minutes later shows the immediate effect of gravity. The milk has gravitated to the bottom of the stomach, forcing the gas to the upper part of the fundus, and it was now *possible* for the first time for the gas to escape. After this exposure the child was patted on the back rather forcibly and he cructated gas several times. This was done easily and no milk was vomited. The entire aspect of child changed at once. He stopped crying and went to sleep. Figure 9 shows his stomach five minutes later (ten minutes after feeding). The stomach has lost all of its gas except a small bubble just at the cardia, which is overlapped by the liver shadow. The stomach has contracted down on the milk and small amounts of bismuth have entered the small intestines. The child was then again put on its back. Figure 10 shows the stomach contracted down on the milk and illustrates its oblique position from above downward and forward to the right. The contrast between Figures 7 and 10 is as striking as was the contrast in the aspect of the infant.

The horizontal prone position is better than the supine, because the liquid food gravitates to the anterior part of the stomach and forces the gas to the posterior part. This places the cardiac orifice above the level of the fluid, and makes it possible for the gas to escape by the esophagus. This is perhaps the reason why so many infants sleep better "on their stomachs" than on their backs.

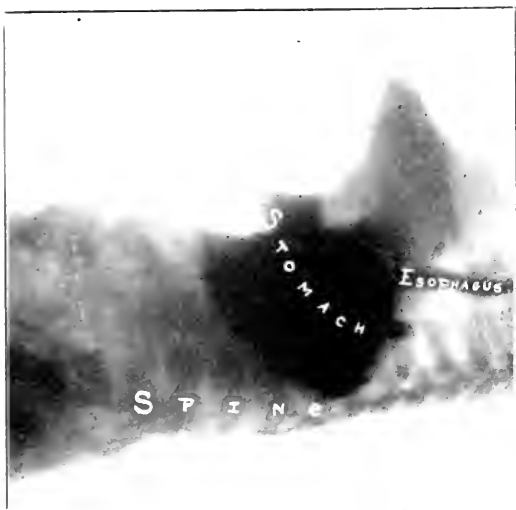


Figure 7



Figure 8

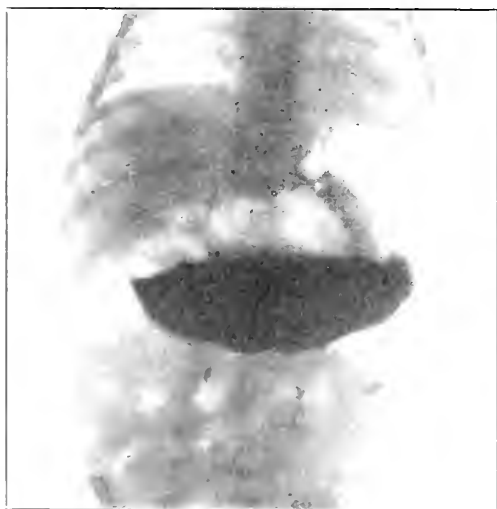


Figure 9



Figure 10

Fig. 7.—Healthy child, aged 6 months; shown also in Figures 8, 9 and 10. Given usual feeding of 6 ounces plus $\frac{1}{2}$ ounce of bismuth subcarbonate. Feeding taken eagerly in ten minutes; considerable air swallowed with it. Position horizontal during and after feeding. Plate made three minutes after feeding. Child held in supine position, left side against the plate. Child very uncomfortable; vomited during first exposure. Milk and bismuth are in the posterior part of the stomach, gas in the anterior part. Esophagus is shown well below the level of the fluid, lying on the bodies of the vertebrae. Considerable gas in the intestine.

Fig. 8.—Five minutes after feeding. The child was held in the erect position, the anterior abdominal wall held against the plate. The gas has been forced upward to the upper pole of the stomach by the fluid which has gravitated to the lower part. After this plate the child was held upright, and was patted on the back. He eructated gas twice in considerable amounts. He immediately became more quiet, stopped crying and went to sleep.

Fig. 9.—Ten minutes after feeding. Position same as last plate. The gas has all been expelled from the stomach except a very small bubble just at the cardia, that is, just to the left of the vertebral column. The stomach is contracting down on the food. The splenic flexure contains a good deal of gas. This was overlapped by the stomach in the last picture.

Fig. 10.—Fifteen minutes after feeding. Position supine, left side against the plate, as in first plate. The stomach has contracted, and a peristaltic wave constricts it in the middle. A very small bubble of gas lies between the level anterior line of the fluid and the anterior abdominal wall.

This is shown in the third series of radiograms. Figure 11 shows the same large air-bubble in the anterior part of the stomach, the child being in the supine position. The child was turned over into the prone position and the illustration shows the air-bubble forced back by the milk which now occupies the anterior part of the stomach (Fig. 12). The position of the esophagus does not show, as the child was not vomiting, but it can be determined by noting the bodies of the vertebrae, and remembering that the esophagus lies about 1 cm. from their ventral surface. This is well above the level of the liquid.

The third picture (Fig. 13) shows the child held erect. He eructated some at once so that the bubble in the fundus end is smaller than in the last plate. He was then placed face downward and a plate made with the rays directed from behind forward (Fig. 14). This is the usual prone picture and shows how impossible it is to estimate the amount of gas present in this position, as it overrides the milk and only shows as a rim at the fundus end. It also shows the mobility of the pyloric end of the stomach, which is here pushed well over to the right of the mid-line (Contrast Fig. 13). The effect of posture and pressure has made two apparently different "types" of stomach.

The child was then held up and eructated gas twice, without vomiting. The next picture (Fig. 15) shows a decidedly smaller air-bubble. The last picture (Fig. 16) taken from right to left in the supine position shows the fundus end of the stomach contracted down on the milk and only a small bubble present toward the pyloric (anterior) part of the stomach. The contrast between Figures 11 and 16 is again striking enough to account for a good deal of difference in the comfort of the child.

If the child is kept horizontal from one feeding to the next the result depends on how much air is swallowed with the food, the capacity of the stomach and the ease with which the child vomits. If a large amount of air is swallowed, vomiting nearly always takes place, usually in the form of simple regurgitation, but occasionally the vomiting may be violent and projectile. Children vary greatly in the amount of air swallowed and in the degree to which the stomach will bear distention. Some will swallow and retain an enormous air-bubble without vomiting, but the usual result is rejection of part of the food by mouth until the tension on the stomach wall is relieved. The effect on the stomach of the extreme distention seen in some cases must be unfavorable to digestion. It seems as if there must be interference with secretion by the pressure on the mucosa and blood vessels. If the gas is expelled, then the stomach is free to contract and secrete. When the child is *kept* in the horizontal supine position the gas is gradually forced through the pylorus, and must traverse the intestine before escaping,

for even if part of the food is vomited the gas cannot escape by mouth. If the gas is in large amount it causes intestinal colic. This symptom may often be entirely relieved by assisting the expulsion of the gas by mouth, so that it need not be passed through the intestine. The symptom of "colic" is probably due in many cases to painful gastric distention, as well as painful intestinal peristalsis. The frequency with which colic accompanies regurgitation is suggestive of their common origin.

Figures 17 to 20 illustrate this point. Figure 17 shows the gas-bubble as usual at the anterior part of the stomach. The child eructated all the gas as soon as he was held upright, so Figure 18 shows no gas in the stomach. Figure 19, in the prone position, shows the change in shape and position of the stomach due to pressure on the abdomen, compared with Figure 18. Figures 17, 18 and 19 all show a large amount of gas in the small intestine. In Figure 20—five hours and twenty-five minutes after feeding—there is still bismuth in the stomach. This child was fed every three hours, so that the second feeding was taken before the stomach was empty and mixed with the residue of the first. The child should have been fed every four hours. The cecum contains almost all of the rest of the bismuth except a small amount in the small intestine. This corresponds to the usual mechanism of a rapid passage of food through the small intestine. The transverse colon is full of gas, namely, that which was in the small intestine in Figures 17, 18 and 19. There is very little gas in the small intestine. This is in accordance with the fact that the gas taken in with the bismuth meal was expelled by mouth, and therefore was not passed through the intestine as would have been necessary if the child had been kept in the horizontal position.

Children vary greatly in their ability to relax the cardia, and eructate, some doing it easily and apparently voluntarily, while others do it only with great difficulty. The instinctive posture which many mothers assume (if not taught otherwise by nurse or doctor), when they hold the baby up against the shoulder after nursing, is the one in which the baby can most easily get rid of this undesirable swallowed air. Patting on the back aids the process of eructation, and it sometimes requires patting of considerable force. Slight pressure on the epigastrium may be needed, the mother grasping the baby's abdomen with her free hand and gently rubbing and pressing the stomach with her thumb, as he rests against her shoulder. At times the eructation may be violent and the contraction of the stomach so forcible and rapid that a small amount of milk comes up with the air. The amount of regurgitation from this cause is negligible, compared to the comfort given the baby by relieving his gastric distention. The air does not always all come up at once, often requiring several eructations. In



Figure 11

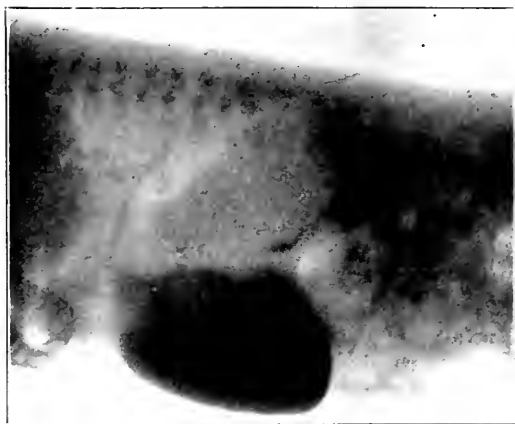


Figure 12



Figure 13



Figure 14

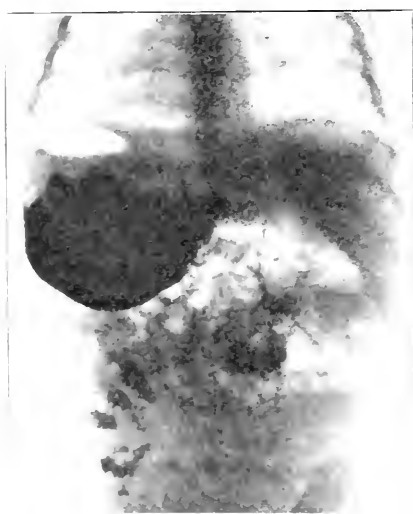


Figure 15

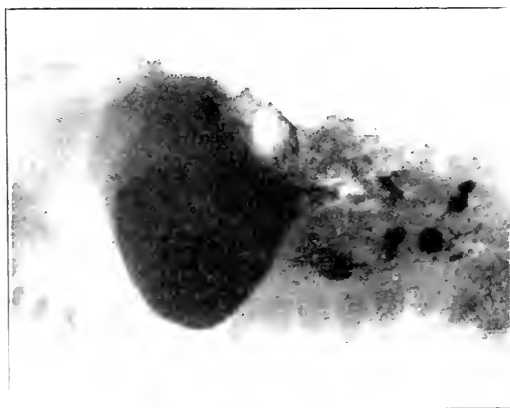


Figure 16

Fig. 11.—Healthy child, aged $6\frac{1}{2}$ months; shown also in Figures 12, 13, 14, 15 and 16. Given usual feeding of $5\frac{1}{2}$ ounces with bismuth subcarbonate $\frac{1}{2}$ ounce. Taken well, no vomiting. Plate made two minutes after feeding was finished. Supine position. Right side against the plate. Enormous bubble of gas in stomach. Fluid line well above site of esophagus.

Fig. 12.—Three minutes after feeding. Prone position. Left side against the plate. The milk has gravitated anteriorly, forcing the gas to the posterior part of the stomach. The position of the vertebrae show that the esophagus is now above the fluid line. The child was then held erect and eructated gas at once.

Fig. 13.—Four minutes after feeding. Erect position. Abdomen against the plate. The air bubble is at the upper part of the fundus, in a position whence escape is easy by the esophagus.

Fig. 14.—Five minutes after feeding. Prone position, the child's abdomen in contact with the plate. Note the gas only as a rim at the fundus end and the position of the pylorus compared with the preceding (Fig. 13). The child was again held upright and eructated more gas.

Fig. 15.—Eight minutes after feeding. Erect position. The gas bubble is still smaller in Figure 13.

Fig. 16.—Nine minutes after feeding. Supine position. Right side against the plate. There is only a very small bubble at the anterior part of the stomach. The stomach has contracted down on the milk. Compare Figure 11.

some cases (as in Figs. 1 to 6) a baby has to be held up every two to three minutes during the feeding to prevent vomiting from air swallowing. It is seldom possible to remove all the gas even when the baby eructates easily, but the small remaining amount causes no discomfort as a rule.

An illustrative case is that of the child from which Figures 1 to 6 were made. This was the second child, a large baby at birth. The labor was easy and short. She was breast-fed for two months, every two hours for twenty minutes. The milk then failed and the mother gave equal parts of milk and water with a "pinch" of sugar in each 5-ounce feeding, given every two hours by day during the third month. About 45 ounces were said to have been given in a day. The child was seen first at three months; weight 9 pounds 6 ounces. The nutrition was not very good, but the child was otherwise in fair condition except for a much-distended abdomen. She had vomited after nearly every feeding since birth, at times violently, but generally had simply regurgitated part of each feeding. The stools were three or four a day, yellow, soft, with occasional curds. She had some colic, and expelled a good deal of gas from the bowels. She slept well from 10 to 6, but the sleep was disturbed during the day. She had been fed in the horizontal position and had been put to bed in that position as a rule, but had occasionally been held up, and had eructated gas. A diagnosis was made of too frequent feeding, too large a total amount, air-swallowing and postural vomiting. The following formula was prescribed:

| | | | | |
|--------------------------------------|------------------|--------------|----------------------|---------------|
| Milk, 4 per cent..... | 18 ounces | 367 calories | Fat..... | 2.4 per cent. |
| Lactose, 3 level table- spoonfuls | | 116 calories | Sugar..... | 6 per cent. |
| Water | 12 ounces | 483 calories | Protein..... | 2.1 per cent. |
| | <u>30 ounces</u> | | Energy quotient..... | 52 per pound |

Fed $4\frac{1}{4}$ ounces every three hours; seven feedings.

The mother was carefully instructed to hold the child erect after each feeding in the routine manner (see summary).

One week later there was no gain in weight; still 9 pounds, 6 ounces. The child still vomited; the mother was discouraged and said the child was hungry. The milk was increased 2 ounces making the formula fat, 2.65 per cent., sugar, 6.3 per cent., protein, 2.4 per cent.; caloric value 554; energy quotient, 59 per pound.

One week later, the child still vomited a great deal, but had gained 14 ounces, weight 10 pounds, 4 ounces. The mother was then carefully questioned and said that the child vomited whether she was held up or left flat, but admitted she had not held the child up after every feeding, but only when the baby cried or seemed restless.

The whole purpose of the routine was again carefully explained and the mother was told to hold the child erect *before feeding, in the middle of the feeding and at the end of the feeding.*

One week later, vomiting was much less; weight 10 pounds, 10 ounces; same formula.

One week later, there was no more vomiting; weight 11 pounds, 2 ounces; same formula.

One week later, there was no more vomiting; weight 11 pounds, 14 ounces; same formula.

General comfort greater, sleep quiet, no colic. Energy quotient 50. The roentgenograms show that this child swallowed an excessive amount of air. During feedings it was possible to hear a gulping sound with each swallow.

Different nipples were tried, and the food was given slowly and rapidly without result. It is evident that this child swallowed as much air in taking 2 ounces of food as the average child does in taking a much larger amount, and therefore it was absolutely necessary that an opportunity be given to get rid of the air in the middle of the feeding, before the stomach became too greatly distended. We believe that this is an example of a large number of cases which are diagnosed as "nervous vomiting," "habitual vomiting" or even as pylorospasm.

Many very feeble babies vomit whenever put down on their backs even if held upright until the gas has all been expelled. The cardiac sphincter seems to have no power, and the milk simply flows out of their mouths whenever gravity has a chance to act. This may be stopped, in some cases at least, by constantly keeping the basket or bed at an angle of about 45 degrees, and never letting the child assume a horizontal position. The prone position may be borne, but it is better to have the head well raised.

The time taken at the bottle or breast is of importance. We believe that it is better for a child to take a feeding too rapidly than too slowly. Rapid nursing may choke the baby and cause coughing, gagging and vomiting if the pharynx fills too rapidly. Slow feeding, that is, twenty to thirty minutes, only multiplies the number of swallowing acts, diminishing the amount of milk and increasing the amount of air taken in each swallow. The old argument against rapid feeding is probably based on cases in which an enormous amount of milk was obtained from very full breasts and regurgitated from *overfeeding*, not from *rapid* feeding. If an infant is weighed every minute while nursing a full breast it is often found that 50 per cent. of the milk is taken in the first two to three minutes, 75 per cent. in the first five minutes and after that the amount per minute decreases rapidly. Such infants show no more signs of discomfort or indigestion and do not vomit more than others, unless they stay at an empty breast sucking and swallowing air. A case may be cited in which a 6-weeks baby obtained from $2\frac{1}{2}$ to 3 ounces in forty seconds and showed no signs of discomfort. The mother had to use a watch to time the feedings. If nursed one minute he vomited from overfeeding. Rapid feeding, therefore, in itself causes no symptoms, and except in the case of feeble infants there is no good reason why a feeding should not be taken in five to ten minutes, or at most in fifteen rather than the traditional twenty.

This is quite contrary to the usual teaching. Nurses are taught that the baby must spend twenty minutes at a bottle. Experience shows that the holes in the nipple must be made very small indeed to prevent a strong child from emptying a bottle in ten minutes. It is much better to have four or five large holes so that the milk runs freely without shaking the bottle when it is inverted, and let the baby regulate the



Figure 17

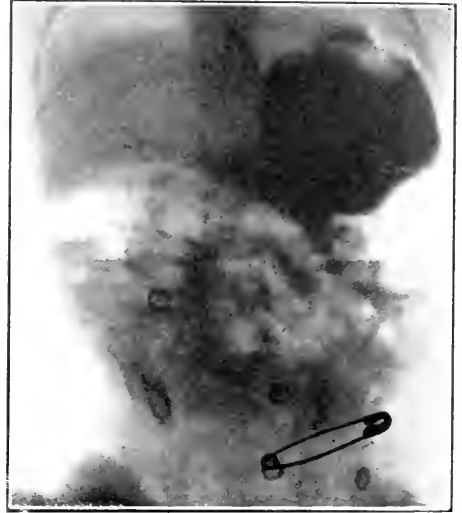


Figure 18



Figure 19



Figure 20

Fig. 17.—Healthy child, aged 7 months; shown also in Figures 18, 19 and 20. More or less vomiting since birth. Given usual feeding with bismuth subcarbonate $\frac{1}{2}$ ounce. Feeding taken readily in fifteen minutes. Child kept in horizontal position. No vomiting or apparent discomfort. Five minutes after feeding. Supine position. Left side against plate. There is a large bubble of gas in the anterior part of the stomach. The milk lies in the posterior position. The small intestines contain a good deal of gas.

Fig. 18.—Eight minutes after feeding. Erect position. Abdomen against plate. As soon as this child was held erect the gas came up as a loud eructation. There is practically no gas left in the stomach, which has contracted down on the food. A little bismuth has entered the small intestine.

Fig. 19.—Seventeen minutes after feeding. Position prone—anterior abdominal wall against the plate. The difference in shape of the stomach between this and Figure 18 is striking. The pylorus has moved well over to the right, probably due to pressure on the abdomen by the surface upon which the child was lying. A good deal of bismuth has entered the small intestine.

Fig. 20.—Five hours, twenty-five minutes after feeding. Erect position. There is considerable bismuth still in the stomach, due to short interval feeding. The rest of the bismuth is in the cecum except for a small amount in the intestine, which contains little gas. The gas which was in the small intestine is now in the colon.

time for himself. Puny infants often become so discouraged at sucking at a nipple with the usual small holes that they will not try to take the bottle at all.

That posture is not without importance in abnormal conditions was shown by a case of pyloric stenosis. This child had a typical history of pyloric obstruction beginning at about six weeks, and had developed a large dilated stomach with tumor, peristaltic wave, projectile vomiting and wasting. The mother refused operation and even hospital treatment. With lavage and careful feeding — at first breast-feeding, then mixed breast and bottle — the child slowly improved, stopped vomiting and began to gain weight. At the time when the Roentgen-ray plates were made the child was 3 months old and gaining slowly. The bottle was not well taken at this time, so only about 2 ounces of feeding with bismuth subcarbonate could be forced down. There was still retention of considerable food in the stomach, and the two ounces of bottle made the child very uncomfortable. The first plate (Fig. 21) was made in the supine position. It shows the great dilatation and the double pouch-shaped stomach. The lower pouch is the pyloric end. The mother wanted to hold the baby upright at once, for she had been carefully taught the importance of so doing. During the time needed to take the first plate the mother became very anxious and begged that the child be held erect. She said: "I know he will vomit, and he has not vomited in two weeks, and I hate to spoil his record."

Her fears were realized, for the child did vomit violently — in a typically projectile manner, just as he had done at the onset of his symptoms. He was held upright immediately after the exposure and at once eructated a large amount of gas. This gas was not only swallowed air, but also the product of gastric fermentation due to stagnation. The residue in this child's stomach resembled kumyss. The child was held erect until the next plate was made (Fig. 22). This was twenty-five minutes later, and during that time he had eructated several times. Figure 22 shows only a small amount of gas in the stomach. The pyloric pouch has contracted down on the milk and a moderate amount of bismuth has entered the intestine. The child was held erect several times before the third exposure and again eructated. In Figure 23 there is almost no gas in the stomach. The intestines are almost free from gas in all the plates of this child. This is the more remarkable since there was known gas production in the stomach. The mother's care to allow the gas to escape from the stomach by the mouth not only was an important factor in stopping the vomiting, but also saved the intestines the necessity of passing the large volume of gas, with resulting colic and distention.

The teaching in practically all training schools for nurses has been that the baby should be kept in the horizontal position after nursing and must on no account be held up, or "moved about." This theory probably had its origin in an effort to counteract the trotting, rocking, jouncing habits of so many mothers—which of course may cause vomiting—the milk being splashed out of the stomach as it would be from a bottle. This does not take place easily, however, unless the child is held horizontally during the trotting or rocking. A careful census has been kept of all trained nurses in charge of infants in the practice of one of us in the last seven years, and only four or five have been found who had evolved the plan of holding the baby erect *as a routine*. A few more have done it at times when the child seemed to have colic or discomfort. Only one nurse has been found who was taught in her training-school that every child should be held up after every feeding.

Nurses train mothers nowadays. A young inexperienced mother takes the word of the trained nurse as law, and when doctor and nurse disagree, the doctor must indeed possess unusual influence over the mother to have an even chance of having his instructions carried out. Small wonder then that most babies are put into their beds to squirm and cry and vomit until enough milk comes up to relieve the distended stomach. After the trained nurse has left, a mother will sometimes pick up the baby and hold him against her shoulder in a desperate attempt to soothe away the colic with a little cuddling and patting. This is done with a guilty conscience at disobeying the nurse's ironclad rule. When the gas comes up and the baby goes to sleep and stays asleep when put back to bed, the mother begins to think. It needs but few repetitions of the experience for the intelligent mother to draw the correct conclusions. Unfortunately, the courage to disobey the nurse's law and the ability to draw conclusions from observation and experiment are rarely combined in one young mother.

Among the poorer classes, where there is no adverse suggestion from the nurse, the baby is often held upright as a routine. It must be admitted that the grandmother is often right on this point, much as she is abused for her interference with modern training and discipline.

Hospital feeding cases are usually examples of the bad results of the horizontal position. In many hospitals the babies are fed in bed and allowed to lie without change of position day in and day out, except when taken up to be bathed or moved to another bed. It is a simple matter to note in practically any case in such a ward that the abdomen is distended, with a large area of gastric tympany. Holding the child erect for a moment will bring up a large bubble of gas, and the percussion note of the epigastrium changes at once. Besides the effect on

the stomach, and on regurgitation, etc., it must be bad for such babies to lie in one position all day. Dr. W. P. Northrup pointed out years ago that it was the lack of holding in the mother's arms which made so many of these children do badly.

Older children who sit up by themselves regulate this matter under ordinary circumstances, but in acute illness, as pneumonia, there may arise a condition of gastric distention due to the horizontal posture. Raising such patients to the erect posture occasionally aids in the eructation of gas and relieves the pressure on the heart and lungs. This is probably one reason why surgical patients do better in the semi-erect position than when the foot of the bed was raised, as was formerly the general practice.

Medical text-books do not mention the posture of the child after or between feedings as a cause of vomiting or indigestion. The matter is dismissed with the general statement that the child should not be moved about after feeding. Medical writers are also silent on this subject with a few exceptions.

Rosenstern,⁴ in a clinical lecture in Finkelstein's clinic, notes the importance of posture. He says that the practice of mothers and nurses of holding infants up and allowing eructations during and after feeding is regarded by doctors as an evil and is not described in medical text-books, but is found in a few written by nurses. He quotes Wilhelmina Voelzter to the effect that children held up vomit less and sleep better. He also notes that often young children after drinking a while get too full and can hold no more, become uncomfortable and if forced they vomit. If held up after a few minutes they eructate, and often a large amount of air. They will then take more food. This is especially true of children fed on dilute milk mixtures, in the early months, and in hospitals where nurses have no time to hold babies up.

Usener says:

Daily experience teaches us that nurslings who are held up by nurses one-half to one and one-half hours after feeding almost always eructate more or less gas. Many mothers and good nurses hold the baby up during or after feeding from the experience that they take the feeding better, vomit less and are more quiet if they have eructated.

Kilmer⁵ advised holding babies upright for colic to let the bubble which caused the colic escape.

Tweddell⁶ says that after feeding the baby may be picked up if restless, held against the shoulder and patted gently on the back for a minute or two, as a little wind on the stomach may be the cause of the restlessness.

4. Rosenstern: *Deutsch. med. Wchnschr.*, Sept. 26, 1912, p. 1834.

5. Kilmer: *Practical Care of the Baby*, F. A. Davis Company, 1903.

6. Tweddell: *How to Take Care of the Baby*, Bobbs-Merrill, 1913.



Figure 21

Fig. 21.—Child with pyloric stenosis, aged 3 months; shown also in Figures 22 and 23. Onset of symptoms at 6 weeks. Classical symptoms of stenosis or extreme spasm with gradual relaxation of spasm and improvement. Child doing well at this time, but stagnation and fermentation still taking place. Took bottle badly, only 2 ounces of food with bismuth subcarbonate 1:8. Five minutes after feeding. Supine position. Left side against the plate. Huge gas bubble anteriorly. Double pouch of stomach well shown. Child vomited violently just after exposure. Child was then held erect and eructated large amounts.



Figure 22



Figure 23

Fig. 22.—Twenty-five minutes after feeding. Erect position. Abdomen against the plate. There is only a small gas bubble at the cardiac end of the stomach. Considerable bismuth has entered the small intestine. The child was held upright several times during the next half hour and eructated more gas.

Fig. 23.—One hour and fifteen minutes after feeding. Erect position. There is very little gas left in the stomach. The intestines in Figures 22 and 23 show little or no gas. This is instructive in this case with known gas formation in the stomach.

Grullee says:

Colic immediately after feeding is probably from stomach, later from intestinal gas. To expel the stomach gas the child can be held to the shoulder or across the lap.

CONCLUSIONS

Air is swallowed with the food by many if not by all infants.

The erect posture favors eructation of this air; the horizontal posture prevents it.

The horizontal posture, by preventing eructation, is an important cause of vomiting, colic, indigestion and disturbed sleep.

The following routine should be followed in feeding every infant:

Before feeding the infant should be held upright to allow the escape of any gas present in the stomach.

Immediately after feeding the infant should be again held up against the shoulder of the mother or nurse. He may be patted on the back or gentle pressure may be made on the epigastrium to encourage eructation of the swallowed air.

It may be necessary to interrupt the feeding one or more times to hold the child upright to eructate, in cases in which an excessive amount of air is swallowed.

After the gas is eructated the child should be put down to sleep, preferably in the prone position and with the head of the bed raised.

If restless he may be taken up after a short time to see if there is more air in the stomach.

Habitual tongue-suckers need to be held up several times between feedings, as they constantly swallow air. Other suckling habits must be prevented by mechanical restraint.

Feedings should be given at as long intervals as possible, depending on the gastric capacity and the total daily requirements.

A feeding should not be taken too slowly. From five to ten minutes are enough as a rule; fifteen minutes should be the maximum time at bottle or breast.

The importance of posture and the wrong teaching given to physicians and nurses in the past warrant the emphasis laid on so simple a matter.

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MEGACOLON AND MICROCOLON *

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Pediatricians express difference of opinion as to the relative frequency of megacolon. Some authors of wide experience are able to make reports on only one or two such cases; that such experience is not general is attested by the fact that in the literature of the past four years there are more than one hundred papers each of which deals with one to six cases. It follows, therefore, that the affliction cannot be extremely rare. We have encountered six cases during the past five years; two of these passed from observation after one view and, therefore, are not included in this report. Microcolon, on the other hand, seems to be truly an unusual condition, as our search through the literature revealed but three certain and one doubtful case, although it seems probable that some reports under the caption "Stenosis of the Colon" may have referred to this condition.

The name "megacolon" has been used to describe the clinical picture characterized by obstinate constipation, great abdominal enlargement, visible intestinal peristalsis with the constitutional results of toxemia due to fecal retention. Constipation at times causes such retention of feces that fecal masses accumulate; these may shift and cause attacks of acute or subacute obstruction of the bowel. The literature referring to this congenital enlargement of the colon is ample. In his masterly article written in 1908, Finney presents a bibliography of 206 titles compiled by A. W. Fisher, complete to the time of his writing. We have searched the libraries diligently and find that over 100 papers on the subject have appeared since Finney's writing. One of the best of these later articles was written by Barrington-Ward and published in January, 1914. One must agree with Barrington-Ward's statement that Finney's paper so completely discusses all phases of the disease that it must remain the authoritative communication on this subject for a long time to come.

Although Finney shows that some twenty odd cases, one by Lewitt of Chicago (1867) and another by Jacobi, were clearly described before Hirschsprung published his studies of the malady in 1896, we owe the eminent Dane a debt for centering attention on the importance of the condition. This writer classified giant colon as: (*a*) true megacolon, first noticeable at birth or early infancy; (*b*) pseudomegacolon, making its first appearance in adult life and showing dilatation of the

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colon with hypertrophy of its muscle, and arising secondary to some partial obstruction that came on during the postnatal period. Many writers deny pseudomegacolon pathologic validity, and, in fact, there seems to be little common to the two conditions.

Barrington-Ward divides the theories which seek to explain the origin of megacolon into four classes: (1) the mechanical; (2) the neuropathic; (3) the inflammatory and (4) the congenital. Under the mechanical theory he arranges five subheads: (*a*) the view of Barth, that an increased mesentery permits torsions of the sigmoid with partial occlusion and subsequent hypertrophy and gigantism of the intestine; (*b*) the view of Marfan, that the increased length of the intestine, especially the sigmoid portion, throws the bowel into a loop which causes kinking obstructions; (*c*) Treves' view, that the obstruction follows atresia of the anus and rectum; (*d*) Perth's idea, that valve formation is the cause of the obstruction; (*e*) Wilkie's conception, that the primary obstruction is due to the distention of the pelvic colon with meconium at time of birth or shortly after. As will be seen, none of these theories makes the difficulty of interpretation less.

Four different explanations are offered in elucidation of the neuropathic theory. It is suggested: (*a*) that there is a neuromuscular defect of the segment of the intestine; (*b*) that there may be a paralysis of a segment of the intestine; (*c*) that there is some implication of the sympathetic nervous system, and (*d*) that reflex spasm of the sphincter ani, a result of a fissure in ano, is the basic cause of the trouble.

Adherents to the third theory hold that a colitis that later becomes chronic originates those pathological processes which afterward produce the full picture of megacolon.

The proponents of the fourth theory assign the only cause which seems to explain the known facts. They hold with Hirschsprung that the condition is an anomaly of development and that the hypertrophy and dilatation both occur in the fetal intestine before birth. Concetti, while acknowledging the congenital origin of the dilatation, considers that the hypertrophy follows effort made to overcome the obstruction due to an inert segment of the dilated bowel. Other writers, among them Fenwick, believe that the hypertrophy is the congenital feature, and that the dilatation is the result of the pressure of the retained gases. In favor of the theory of congenital origin are age at onset, presence of constipation and other symptoms from birth as illustrated in all the cases here reported as well as by a study of the pathology. Furthermore, cases have been reported in which fully developed megacolon occurred in prematurely born children.

Barrington-Ward points out that developmental errors are most common at the junction of the proctodeum and hindgut and that the site of next greatest frequency is at the junction of the foregut and midgut. He considers that in megacolon the developmental error occurs at the former site, and he draws attention to pyloric stenosis as a possible example of developmental error in the later position. It is well known that the increase in the length of the intestine during the last month of intra-uterine life is usually about 25 per cent., but that there is great individual variation in this respect. At birth the infant's intestine is at least one-tenth longer in proportion to the body length than is the adult's. Much of this increase goes to make the sigmoid of excessive length in the infant. In the normal baby, growth rapidly balances this relationship, but in cases of giant colon such balancing is impossible, at least in well-developed cases. From such facts Finney infers that the colon is still under morphogenetic evolution, that the inconstancy of its length and minor details are but variations in the progressive evolution toward the final arrangement, and that the anomalies are but reversion types. According to him, in megacolon all the segments of the intestine may be involved, but more often the condition concerns that segment whose evolution is most primitive. He lays great stress on the thickness of the mesocolon in one of his cases. This he states to have been the result of enlarged lymph-glands together with enormously dilated lymph and blood vessels, which corresponded exactly with the gigantic section of the bowel. This appearance suggests to him a state of hypernutrition and he calls attention to the fact that this same increase in vessels is a feature of that gigantism which occurs in the limbs; he suggests that the conditions in the bowel may be parallel. A reference to the photomicrographs will show that in our cases very large much-dilated vessels occurred not only in megacolon, but in pyloric stenosis and in giant small intestine as well. But none of our material showed the lymph-node hyperplasia that Finney found in his case.

Briefly stated, Barrington-Ward's theory, which seems the most explanatory, is that there is a congenital abnormality in the lower end of the hindgut which takes the form of a muscular hyperplasia. It usually involves the rectum and spreads a varying distance up the pelvic and iliac colon. It may be that the whole of the hindgut is affected, but in some cases there is a definite localization of the change and the hyperplasia affects only a segment of the intestine. The hyperplasia of the muscles gives rise both to thickening of the walls and to increase of the bowel lumen. The physiologic functions of the intestine are in abeyance, and blocking is produced in the bowel behind, for a varying distance, which depends on the extent and duration of the

dilatation and hypertrophy. In time this fecal stasis produces necrotic changes in the mucosa, an ulcerative colitis follows which is the cause of death in most instances. It seems reasonable to us that Barrington-Ward and Finney each contribute facts that, taken together, explain the underlying causes of the pathology in these conditions.

CASES OF MEGACOLON

The following cases of congenital enlargement of the intestine are reported because they serve, some to throw light on the disputed points, and others to illustrate the danger of temporizing management, while the last case shows the efficacy of operative interference. The case of microcolon is included not only because of its rarity, but because it illustrates a condition opposite to megacolon and at the same time furnishes us with an abnormality in the small intestine which in every way parallels the pathological changes found in the large intestine in cases of giant colon. We present for comparison the photomicrographs of the giant colon, of the hypertrophied small intestine and of a case of hypertrophic pyloric stenosis. A comparative study of this picture will show how nearly identical the muscle and blood-vessel changes are in the three conditions. Our cases of megacolon are as follows:

CASE I.—Baby S., referred by Dr. A. B. Spalding. Seen on the fourth day of life. The mother and father were healthy people. The birth normal, at full term. The child was brought in because of increasing abdominal distention and because the bowels had not moved since just after birth, when a small amount of mucus and meconium-like material was passed. No one had noticed the passage of any flatus.

On admission, the child weighed 8 pounds. It appeared somewhat dried-out, the skin hanging loose and lusterless. The child was well formed with no deformities except that the abdomen was exceedingly prominent. This enlargement was especially marked when contrasted with the dried-out limbs, and was taken to be due to gas retention. It was noted that there was an area of visible intestinal peristalsis which passed across the abdomen from the left iliac fossa to the border of the ribs on the right side. This area was horse-shoe-shaped and seemed to be due to movements in two separate segments of the intestine. The upper segment showed movement from left to right, while the movements in the lower segment appeared to pass from right to left. On examination the heart and lungs were normal; no tumors were determined in the abdomen. The abdomen was distended but not hard and was easily palpated. The anus was patent; the little finger entered an apparently normal rectum but was arrested just above the brim of the pelvis by what felt like a narrow band.

The child retained milk from one-half to one hour and then rejected it all. Attempts to give enemas were unsuccessful; the water returned uncolored. A bismuth meal was given and the child radiographed by Dr. Boardman. In the picture the stomach appeared normal, but the plates taken one and two hours after the meal showed no retention of bismuth in either stomach or intestine; all had been vomited. The child was kept alive by hyperdermoclyses of 4.5 per cent. glucose in normal salt solution.

Based on the finding in the rectum of a definite narrowing and of an apparent obstruction to the exit of the bismuth meal from the stomach together

with visible peristalsis, a diagnosis was made of multiple stenosis of the intestinal tract with narrowing at the duodenum in the small intestine and at the pelvic colon.

A surgeon was asked to see the child and to attempt multiple anastomosis. When the abdomen was opened the true state of affairs was revealed. A giant colon bulged into the wound and was returnable with great difficulty. The area of peristalsis proved to have been produced by a long redundant loop of the sigmoid which stretched across the abdomen. The outgoing loop crossed the transverse colon as high as the pylorus; it then wound around the lower



Figs. 1 and 2.—Patient 3, three months before death from pertussis.

border of the liver, and the incoming loop, starting above the hepatic flexure, ran thence to the left iliac fossa, where it terminated in a distinctly narrow but slightly hypertrophied area about $1\frac{1}{2}$ inches in length. The child succumbed to the operation. Necropsy confirmed the findings revealed at the operation.

Unfortunately, the removed intestine was lost, hence it is impossible to report on the microscopic conditions present in this specimen.

This case is of interest in that it shows true giant colon to be a condition that may present itself at birth with fully developed dilatation and hypertrophy — this in spite of the view of those authors who

hold the dilatation to be variable and secondary, and others who have a like opinion about the hypertrophy. It is further of interest because, had the diagnosis been made and the intestine promptly opened for drainage, the child might have survived, and a later attempt could have been made to remove the large intestine, as has been done by Arbuthnot Lane. The way in which young children respond to gastro-enterostomy for pyloric stenosis is warrant for the faith that this child might have survived operative interference.

CASE 2.—A. H., 18 months of age. Seen in the course of private practice with the history of having had obstinate constipation and "big stomach" since the fourth month. He was the first and only child, born at full term, after protracted labor. The child had been difficult to feed in that he had not

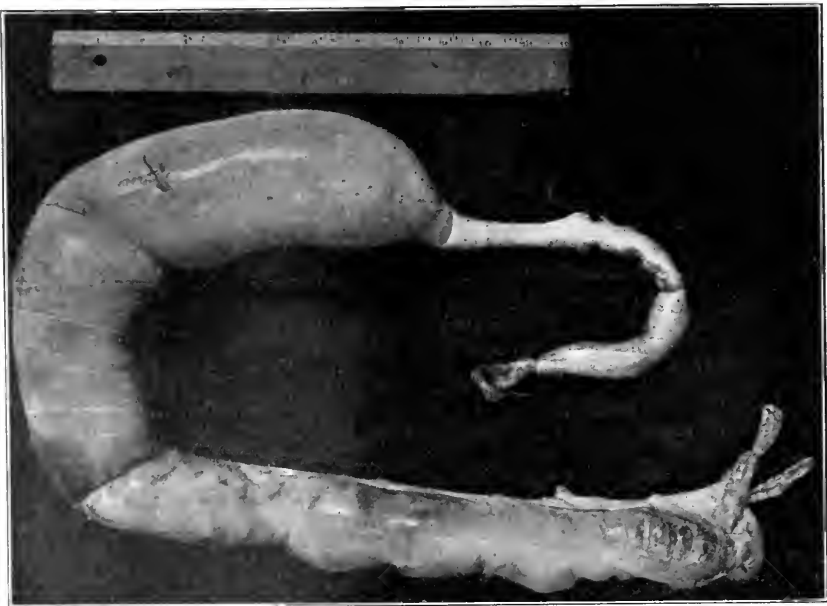


Fig. 3.—Colon from Case 3.

thriven on varying formulas and was astoundingly constipated. On one occasion, during the sixth month, he had passed several days (the mother said ten), without evacuation, and on many occasions there were periods of from two to five days without bowel movements. At such times the abdomen became tremendously enlarged beyond its ordinary huge size and the child would suffer attacks with rapid, shallow pulse, embarrassed breathing, and threatened collapse. The mother had learned that by the aid of a soft rubber catheter she could manipulate the contents of the bowel and so greatly relieve the child of the accumulated gas, and with this maneuver she carried the patient through many such crises. She had also discovered that the blocking of the bowel by feces was relieved and the gas most readily passed when the child's hips were held high above the shoulders. It is possible that in this position the retained mass was freed from the narrowed sigmoid by the aid of gravity.

On examination there was revealed an emaciated child with a huge abdomen, measuring twenty-four inches at the umbilicus, and looking, as one colleague

remarked, like a balloon tied to a little skeleton. The skin was dry and hung in folds everywhere except from the abdomen. The distention of the abdomen was exaggerated at the flanks, where the bulging was extraordinary. The diaphragm was high, and the costal region very wide. No visible peristalsis was noted. Masses, hard but doughy, were felt in the abdomen, one the size of a large orange on the right above the navel, another in the left iliac region about the same size, and smaller ones lay in what seemed to be the line of the transverse colon. These were moved about and felt with difficulty because of the extreme distention. Rectal examination revealed a wide, lower rectum, the little finger was stopped at about the pelvic rim by what seemed a definite

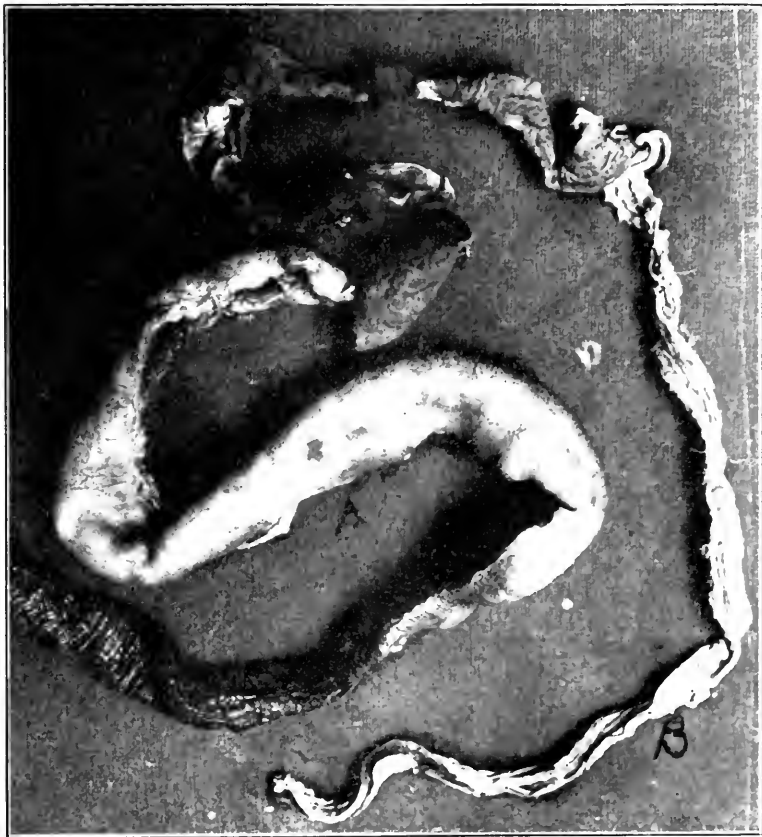


Fig. 4.—Intestines from case of microcolon. *A*, gigantism of small intestine; *B*, microcolon.

narrowing. Bimanual palpitation defined a tumor in the left iliac region, but pressure could not force it downward through the constriction.

The child now entered the Lane Hospital and it was decided to wait twenty-four hours and then to create an artificial anus. The patient seemed in excellent condition. Glycerin and water enemas were ordered and an attempt was made to produce evacuation. Several such enemas were given without result in the course of twelve hours and each time all of the fluid was returned unstained, according to the nurse's report. Apparently, however, a mass of

feces in the transverse colon was dislodged and dropped down into the narrow part of the intestine, where it produced an acute obstruction. At about 10 p. m. on the day of the child's entrance into the hospital, one of us was summoned hurriedly to find the child *in extremis* with the pulse running shallow and uncountable, the face gray, the lips blue, and the patient barely conscious. There was the most tremendous distention conceivable. In the absence of Dr. Weeks from San Francisco, a hurried summons was sent to another surgeon, but before he could reach the operating-room the child was dead. Obviously, the thing which should have been done was to incise, draw out the intestine and open. In the absence of surgical experience, and in the hope of finding skilled aid at once, one unskilled in surgery hesitated to assume this responsibility, but, undoubtedly, if such an emergency were faced again, the opening would be made without hesitation.

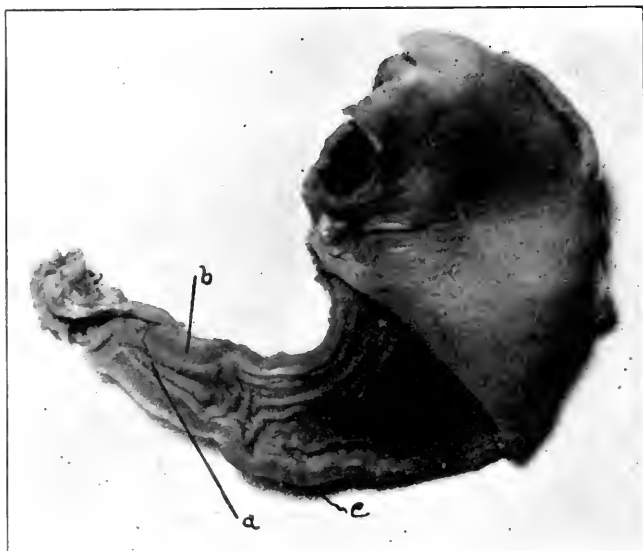


Fig. 5.—Hypertrophic pyloric stenosis, from photograph, full size; *a*, narrowing of lumen; *b*, ring muscle; *c*, hypertrophy of circular muscular coat of stomach. The narrow lumen of the pylorus is seen to be almost completely occluded at *a*. The wall of the pylorus is seen to be greatly thickened at *b*, and is continuous with the hypertrophied musculature of pyloric antrum.

Necropsy was denied us in this instance, so our only help from it lies in the illustration of the potential dangers of the condition and in the emphasis it puts on the view that the only safe procedure in these cases is to make a preliminary colotomy with artificial anus at the earliest possible moment, so that the intestine may be emptied of its retained material. After such procedure the poisoning ceases, the child's nutrition improves, and, with a wait of from two to four months, the physical conditions are so mended that there is warrant for a resection of the entire large intestine with the hope of permanent cure.

CASE 3.—E. S., male, 19 months of age, weight 15 pounds and 4 ounces, seen in consultation with Dr. Dudley Smith (Figs. 1 and 2). Full term, normal birth, birth weight $7\frac{3}{4}$ pounds. The abdomen was so distended at birth that the parents thought the child's hips were deformed because of the great contrast. Constipation at that time was very marked, and there was no evacuation until the fourth day of life, when scybalous masses of hardened meconium were passed, but in small quantity. In the second month a period of nine days elapsed without any movement of the bowel; the abdomen was greatly distended, and the child was much distressed. Evacuation was finally accomplished by enemas and castor oil, but these agencies produced only small marble-like scybala. At the time of this attack no signs of collapse supervened with the distention. The physician then in charge considered the condition to be due to unsuitable food, and the child was subjected to numerous changes in diet without effect. He gained slowly in weight and strength, but such attacks as just described recurred almost every month. On one occasion in the fourth month there was marked diarrhea which lasted for a week and was accompanied



Fig. 6.—High-power photomicrograph of the hypertrophied ileum. The normal mucosa is seen at *a*, under which lies the somewhat thickened submucosa. The muscular layers (*b* and *c*) are hypertrophied, especially the internal coat. The serosa, lying external to the muscular layers (*c*) is edematous.

by depression and great distress, which was relieved by castor oil and turpentine enemas. At six months, after obstruction of four days' duration, a characteristic attack supervened with pain, distention and collapse; at the eighth month another similar attack came on.

Dr. Dudley Smith now saw the child for the first time. He was able to effect evacuation of the bowels and to keep the child in fair condition by large doses of magnesia and the passage of a soft rubber catheter, which effectively relieved the distention. The child's nutrition began shortly to improve; his weight curve commenced to ascend and he reached $19\frac{1}{4}$ pounds in the seventeenth month, in spite of the fact that severe obstructive attacks occurred during the fourteenth and sixteenth months. During the eighteenth month the boy's weight fell during such an attack to $15\frac{3}{4}$ pounds, when one of us saw him for the first time and we coincided with Dr. Smith's opinion that oper-

ative interference held the only promise of relief for the condition. This help was not to be, however, as the child was even then in the first stage of pertussis, to which he later succumbed. The necropsy revealed a typical megacolon (Fig. 3).

The physical examination of this child showed simply a distended abdomen in a rickety subject who exhibited visible peristalsis over the middle and upper section of the abdomen; there were palpable fecal masses, and the rectum on examination revealed a narrowing at the pelvic brim. This case, like the last, shows the method of obstruction that occurs in this pathologic state and in each instance, the pain, collapse, and obstruction were relieved after the passage of a hard, narrow fecal mass which apparently had lodged in the narrowed sigmoid.

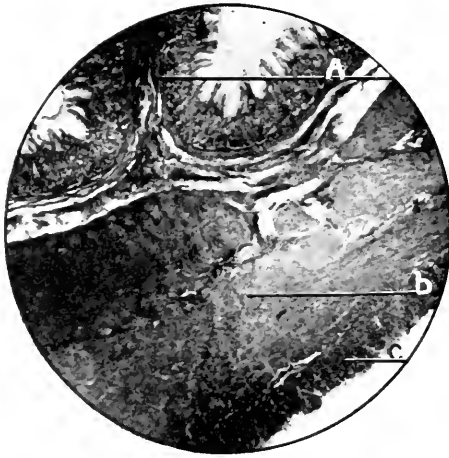


Fig. 7.—Photomicrograph of hypertrophied wall of pyloric antrum. The mucosa (*a*) is normal and is covered with a layer of mucus. Beneath it lies the submucosa, which is loosened from the underlying internal muscular coat (*b*), which shows a marked hypertrophy. Throughout it are seen fibrous connective tissue strands extending down from the submucosa. The external muscular layer (*c*) is not much thickened.

CASE 4.—E. P., male, 22 months of age, referred by Dr. Hughes of Sonoma, Cal., with the diagnosis of Hirschsprung's disease. This was the second child, full term, normal birth. Parents and other children normal and in good health. Symptoms were not noticed by the parents until the fourth month of life. From that time the history was like that of the other cases reported, malnutrition and difficult digestion with attacks of obstruction and collapse. On examination we were confronted with a yellowish gray-skinned anemic child, weighing 22 pounds. There was an enormous abdomen, which measured thirty inches at the level of the umbilicus. We saw no visible peristalsis on this occasion, and there was no such tenseness of the abdomen as had been met in the other cases. Palpation of the abdomen revealed several tumors; the largest, the size of a fetal head, lay in the right iliac fossa, extending upward and toward the right where the bulging was marked. Other similar masses lay above the umbilicus and to the left of it. The largest mass was

smooth, easily movable and was taken to consist of feces lying in the caput coli. Rectal examination revealed no narrowing; on the contrary, the rectum and colon were very large and roomy. Previously, a diagnosis of tuberculous mesenteric adenitis had been made. Bimanual examination with the finger in the rectum revealed a smooth, velvety peritoneum and contradicted this assumption.

Dr. Weeks now saw the child for the first time and advised operation, proposing a two-stage procedure. At the first operation the abdomen was opened on the left side and an artificial anus was created. The method of Levison of San Francisco was utilized and the retained fecal masses were then evacuated and we found that the one which had been discovered on the right side was lying, not in the caput coli, but in the redundant loop of the huge sigmoid. This giant sigmoid crossed over the abdomen and filled most of it; it overlay the apparently normal caput coli and thus gave rise to the erroneous impression. The operator drew the intestine down as far as possible into the left iliac fossa, where it was fastened, opened, and its contents evacuated. The child did well, the toxic symptoms manifested in the dry, yellow skin, anemia.



Fig. 8.—High power photomicrograph of megacolon. The mucosa at (a) is normal. The submucosa (b) is markedly thickened and fibrous and contains many large dilated vessels filled with blood. The muscle layer (c) is also thicker than normal.

and poor nutrition gave way, and at the end of six weeks the child had gained 12 pounds in weight. For four months evacuation was through the artificial opening, then as the child had made such great improvement, it was decided to resect the intestine. This was done at the Children's Hospital in San Francisco. Under ether the redundant sigmoid and the intestine above it up to what appeared to be the normal first part of the transverse colon were resected. After removal this redundant loop was 15 inches in length and in diameter about 3 inches, and its walls about $\frac{5}{16}$ of an inch in thickness. The freed upper end was stitched into the severed end of the rectum; this was accomplished with great difficulty because the rectal tissues were thick from hypertrophy and the tube at that point was nearly three times as wide as was the implanted end of the large intestine.

The report of the microscopic section (Figs. 10 and 11) by Jean Oliver is as follows: "The sections show a normal mucous membrane with well-marked lymphoid follicles which are somewhat hyperplastic. All the muscular elements of the intestine are markedly hypertrophied, including the muscularis mucosae.

The submucosa is rather fibrous and the submucosa and serosa normal. Many large dilated blood-vessels filled with blood are found."

The anastomosis was successful except that there was a small area of imperfect union which gave rise to a slight fecal fistula. This opening, however, closed spontaneously after about two weeks and the patient went on to apparent recovery with occasional attacks of retention of feces and moderate



Fig. 9.

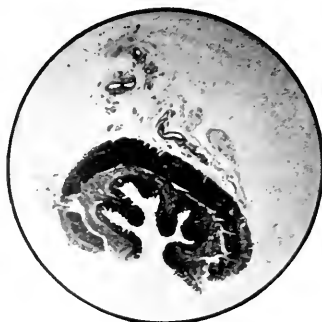


Fig. 10.

Figs. 9 and 10.—Low-power photomicrographs of the microcolon (Fig. 10) and the dilated and hypertrophied ileum (Fig. 9) showing the relative size of the gut of the different levels and the thickness of its walls. The marked dilatation of the ileum (Fig. 9) masks to a certain degree the hypertrophy of the muscular coats so that they do not appear much thicker than those of the microcolon (Fig. 10).

abdominal distention, which were apparently due to the fact that the huge rectum was deficient in tone and expulsive power. For some months the improvement was marked and progressive, but at no time has the patient done so well as during the period while he carried a freely opened artificial anus.

The bowels have to be evacuated by the aid of small low enemas of glycerin or soap and water. This dislodges what appears to be a normal fecal mass from the rectum and each enema is followed by a normal-appearing evacuation.

Six months after the operation the mother stated by letter that some distention was recurring. This is undoubtedly due to the fact that the portion of transverse colon which was left suffered from the same pathologic defect as the portion amputated, although probably to a less degree, and this region is now giving way under the stress of pressure. It seems probable that the remaining colon will yet have to be removed.

CASE OF MICROCOLON WITH HYPERTROPHIED SMALL INTESTINE

During the period of our interest in megacolon Baby R., male, 5 days of age, was brought into the Lane Hospital *in extremis*, deeply jaundiced and cyanotic, incessantly vomiting, ejecting meconium-like material. The child had had no evacuation since birth, had taken but little food and had passed urine a few drops at a time only. The vomiting had persisted for forty-eight hours before entrance. The abdomen was distended and tense; it was possible to diag-

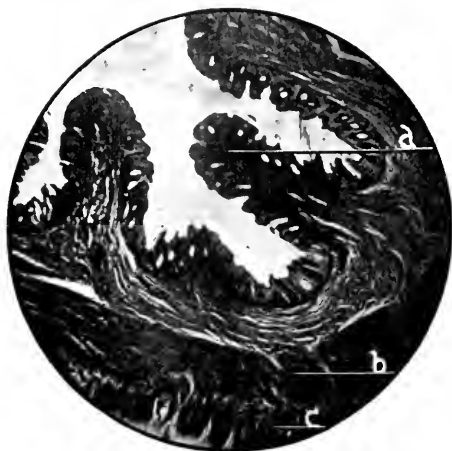


Fig. 11.—High-power photomicrograph of microcolon. The mucosa (*a*) is normal, and the underlying submucosa is somewhat fibrous. The muscular layers (*b* and *c*) are relatively thicker than normal, but the decrease in the size of the intestine is evident in all its layers, no single layer being decreased at the expense of the others.

nose the presence of free fluid in the peritoneal cavity. The anal orifice was normal and the little finger moved freely into the rectum and was stopped just above the pelvic brim by a marked narrowing. A diagnosis of intestinal obstruction due to stenosis at the sigmoid was made, but the child was past aid and died an hour after admission. The necropsy was performed by Dr. William Ophüls, whose notes are as follows:

"Strongly built, male baby, 54 cm. in length. Cyanosis. Anus well formed, patulous. No obstruction in any of the natural orifices. Skin shows yellowish hue all over.

"Some gas in peritoneum and about 350 c.c. of distinctly fecal fluid. Peritoneum is inflamed and covered with soft greenish shreds of fibrin. Omentum is small, hyperemic, contains no fat. Transverse and descending colon very thin and contracted. Sigmoid flexure is pulled up out of pelvis to a certain extent and fastened by vascular adhesions to the mesentery of one of the loops of small intestine. These adhesions are below the point of greatest distention of the bowel. About 10 cm. above the ileocecal valve is a small perforation.

"Upper part of small bowel distended with gas, lower part very much distended; diameter of intestine below is 3.5 cm. in places. Further down distention decreases, increases again, and at the ileocecal valve the intestine has normal diameter.

"Above-described adhesion is below the point of greatest distention of bowel; about 10 cm. above the ileocecal valve is an oval perforation, about 5 mm. in diameter, situated close to the mesenteric attachment, through which fecal matter escapes.

"Upper part of the small bowel is filled with soft greenish brown fecal material. In lowest part of small bowel is thick, pasty material. The ileocecal valve is open. The large intestine is very much contracted. It is almost empty but in some places there is a small amount of dried-up mucus. The rectum is of normal caliber, its mucous membrane hyperemic, with some blood in rectum. Appendix is normal. In region of perforation mucous membrane shows marked hyperemia and extensive hemorrhages, and there is some evidence of necrosis of the mucous membrane. Very much distended part of lower small intestine shows well-marked hypertrophy of muscular wall, being almost 4 mm. thick in places. Mucous membrane is distended, part much inflamed, superficial erosions in places. Necropsy findings revealed no other abnormalities."

Sections were made from the hypertrophied areas of the small intestine by Jean Oliver, whose report is here given.

"Section of the small intestine through its enlarged part shows marked hypertrophy of the muscular layers. This is especially prominent when one considers that there is also great dilatation, which tends to obscure the hypertrophy of the walls. The mucous membrane is extremely hyperemic and there are many large hemorrhages, especially in the submucosa. A considerable layer of mucus covers the epithelium. The serosa is also hyperemic and there is beginning cellular infiltration and deposit of fibrin on its surface. The blood-vessels are large, dilated and filled with blood.

"Sections of the microcolon show the same hyperemia and hemorrhages in the mucous membranes but to a less degree. The submucosa is quite fibrous and also shows considerable diffuse hemorrhage. The muscular layers appear thickened, probably owing to the contraction of the intestine. The subserosa shows marked cellular infiltration and there is a heavy deposit of fibrin in the serosa."

The case of microcolon is included in these reports, not only because of its striking contrast to the megacolon cases, but also because there was also present a condition of hypertrophy of the small intestine (Fig. 4) in which the changes in the muscle and fibrous tissues parallel in every pathologic way the changes of the analogous tissues in the large intestine found in the cases of Hirschsprung's disease. It always seemed to us that the innate pathology underlying megacolon is akin to, if not identical with, the changes in tissue found in hypertrophic pyloric stenosis, especially in that form wherein there is general hypertrophy of the circular muscle of the stomach wall as well as of the ring muscle at the pylorus (Fig. 5). This case of microcolon with gigantism of the small intestine provides a true example of the same marked growth of muscle and hypertrophy of fibrous tissue with gigantism of vessels occurring in the small intestine.

Microphotographs of the sections of the three conditions have been made in the standard Pathological Laboratory by Jean Oliver (Figs. 6,

7, 8, 9, 10 and 11). A study of them will reveal how like the muscle affection and the marked hypertrophy in the mucosa connective tissue and vessels is in the three conditions. The photograph of the stomach from a patient with pyloric stenosis also is evidence for this point of view.

The consideration of our cases of megacolon gives some evidence on disputed points. Certain writers have denied the congenital origin of this condition. Our Cases 1 and 3 exhibited symptoms at birth and in Case 1 a typically developed giant colon was revealed by operation and necropsy. Cases have been reported in which giant colon was discovered in prematurely born children.

It has been questioned whether the sigmoid was narrow in all cases, and it has been asked if the true origin of the dilatation and hypertrophy was not an obstruction that blocked the passage with feces and allowed the work of the intestine and the stress on it to be followed by increased production of muscle and ballooning from the retained gas. Case 4 of this series, in which the gigantism included every portion of the intestine to the anus, shows that the sigmoid narrowing is not present in every case. Case 2 is instructive in demonstrating the potential and emergent dangers to life of the condition, and with Case 4 causes us to resolve that in the future even the youngest child encountered with this trouble shall have the benefit of immediate colotomy and an artificial anus. The well-being of Patient 4 during the time he carried an artificial anus was so striking and the operation is so easy that these facts, taken with the well-known tolerance of infants to abdominal interference, make such an operative interference most reasonable, especially when we consider the unhappy course of Case 2 which demonstrated so completely the extreme danger of temporizing and of trying to evacuate the bowel through the rectum in those cases of megacolon with a narrow sigmoid.

As one considers the condition of gigantism in the intestine, the question presents itself: Are there mild cases of the disease? One who deals much with infants cannot but feel that such cases occur, and are not very unusual. There are obstinately constipated infants, who, while not rachitic, have abdomens that bulge inordinately and in whom the bulging for the most part follows the line of the colon and fills out the flanks to a marked degree. Such children are apt to be uncomfortable, to take food badly and to fail in weight, but they are not distressed by flatus. When their bowels are kept free all the symptoms disappear except the ballooning of the large intestine, and growth seems to adapt the children in time even to this visceral enlargement, for the individuals in this group seemed to do well once they are past infancy. The final proof of this contention must rest on

necropsy of such a child who has met death from another cause, as the condition itself is never fatal, nor indeed is it severe. Hertz has called attention to a class of infants in whom roentgenograms show a lengthened sigmoid, and it may very well be that such infants correspond in the group of megacolon to the cases of mild hypertrophy with spasm that we encounter in the pyloric stenosis group.

The proper feeding of infants with congenital enlargement of the colon is of importance and presents difficulties. High fat formulas are not adapted to this condition, as soap stools give more trouble in all classes of megacolon than do other types of stools. Giant colon cases seem to respond to high percentages of dextrin, yet care must be exercised, as fermentation and gas formation have to be discouraged. Enemas are on the whole the best means of producing bowel evacuations. Castor oil is to be shunned, as is magnesia. In older children milk should not be given.

The clinical picture of congenital enlargement of intestine and the colon is so characteristic that it seems hardly needful to discuss the differential diagnosis. The one case in our series which led to confusion was that of the new-born infant. The differentiation between multiple stenosis and megacolon in the new-born is certainly difficult, but the character of the peristalsis and the mildness of the digestive symptoms should have been a guide to a proper diagnosis. This case was rendered more difficult by the vomiting, which was extreme, and which probably is a most unusual accompaniment of congenital enlargement of the intestine. The only other condition which might possibly lead to a mistake in diagnosis is tuberculous peritonitis, and this mistake will never be made if the child is examined under an anesthetic by the bimanual method, a finger of one hand in the rectum and the other hand on the abdominal wall. The characteristic smooth feel of the healthy peritoneum instantly excludes the presence of tuberculous inflammation. The gristly fibrous bands and the rolled-up lower edge of the omentum in tuberculous peritonitis give to the examining finger a sensation that is absolutely pathognomonic. (In passing, it may be said that there is no maneuver in diagnostic examination of children of more value than this bimanual rectal examination if it be made while the child is under the influence of an anesthetic.) It is unlikely that any of the abdominal tumors will be confused and hardly possible that the dilatation due to chronic intestinal indigestion in rickety children will mislead one.

It is probable that megacolon is a more common deformity than is generally thought. The symptoms are present from birth. They are: an enlarged abdomen, visible intestinal peristalsis, obstinate constipation, later, anemia and toxemia from fecal retention, accompanied

sometimes by recurring attacks of intestinal obstruction. Pathologic hypertrophy with dilatation may include the entire intestine, or the dilatation may cease at the sigmoid, which will be hypertrophied, but with a narrow lumen. That isolated segments of the large intestine may be affected while most of the intestine remains intact and healthy is to be doubted. Fatal collapse can occur from fecal obstruction, and such obstruction may be brought on by injudicious attempts to empty the bowel. The one measure that promises relief is operative procedure, which may be utilized in either two or three stages: colotomy, with artificial anus (this cannot be done too early in the child's life or in the course of the case), later excision of the entire large intestine with anastomosis from the ileocecal region into the rectum; or anastomosis may be done as a second step and resection of the entire colon be made a third operation.

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A STUDY OF THE NUTRITIVE VALUE OF SOME PROPRIETARY INFANT FOODS

II. AS MILK MODIFIERS *

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URBANA, ILL.

An earlier number of this journal contained a report¹ from this laboratory of a study of the nutritive value of four commercial infant foods, two containing milk and advertised as complete foods, and two made chiefly from grains and advertised as milk modifiers. The object of that investigation was "to study the nutritive value of the foods in themselves," "not cooked nor mixed with milk as such foods are commonly given to babies, but as nearly as possible as they come from the manufacturers, with only such modifications² as are necessary to adapt the food to the species of experimental animal chosen." The necessary modifications were made in all cases by the addition of purified casein and the salts of milk in the form of Osborne and Mendel's "protein-free" milk. The two foods made largely from milk sustained entirely normal growth in young animals and long continued maintenance in adults. The two foods made chiefly from grains and containing no milk did not sustain normal growth; one allowed maintenance, the other did not.

In the series of experiments now to be reported, the foods of this latter group, Mellin's Food and Eskay's Albuminized Food, were studied as milk-modifiers, whole fresh milk in varying amounts being mixed with each day's ration (4 gm.) of the food powder and fed to young animals. The object in view has been to find out *in how far* these foods satisfy the nutritive requirements of growth; whether or not they may furnish a significant proportion of the dietary of a growing animal. Various claims are made for the many milk-modifiers on the market. They are perhaps most commonly said (1) to dilute the excessive protein and salts content of cows' milk, and (2) to

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1. Wheeler and Biester: A Study of the Nutritive Value of Some Proprietary Infant Foods, *AM. JOUR. DIS. CHILD.*, March, 1914, 169.

2. Approximate composition of the mixtures fed: Protein, 18 per cent.; salts, 3.7 per cent.; carbohydrates, about 75 per cent.; fat 1 to 3 per cent.

increase the digestibility of milk by softening the curd. Either of these purposes could be served by small proportions of the food powder and might perhaps be as well served by modifiers much more economical than proprietary infant foods. If, on the other hand, these foods may safely form a significant part of the ration, it would be of value to know wherein they fail as complete foods; whether, for example, from the lack of essential accessory substances or from an inadequacy in the proteins contained in them. With these questions answered, the foods could be used to much greater advantage.

The experimental animals used were, as before, albino mice, and the period of their lives chosen for the feeding trials was that of most rapid growth, that is, from the close of the nursing period—the twenty-first day after birth—until after the mice reach sexual maturity at about the sixtieth day after birth, when the rate of growth markedly decreases. In spite of the facts, that the experimental animals used were not babies and that the observed period not the nursing period, it is hoped that the results of the experiments may prove suggestive to pediatricists; for while the nutritive requirements for growth vary decidedly with the species of animal so far as quantitative considerations are concerned, the food substances needed appear to be the same for all the higher animals. This is indicated by the fact that animals of various species have grown normally on an exclusive diet of cows' milk or of egg yolk. It appears that all animals must have certain amino-acid combinations, carbohydrates, salts and probably some accessory food substances; and a food mixture which will not support proper growth in one species of animal, when the amount of protein, salts, etc., corresponds with the proved nutritive requirements of that species, lacks some essential, and may well be studied with great care if it is to be fed as a significant part of the diet of a baby.

In regard to growth requirements during different periods of life, much the same arguments hold. Even quantitatively there is probably much less change in the optimum composition of food as the animal grows than is often supposed. Certainly the same food substances serve for real growth alike in the nursing period and later. The concentration of the food is a somewhat different matter and will be discussed later.

As before, the mice were caged in groups of two or three; white crepe paper napkins were used for bedding and were put into the cages clean every day; twice a week the cages were sterilized by boiling. Distilled water was supplied in inverted bottles. Food was given three times a day, between seven and eight in the morning, at four in the afternoon and between eight and nine in the evening. At first there

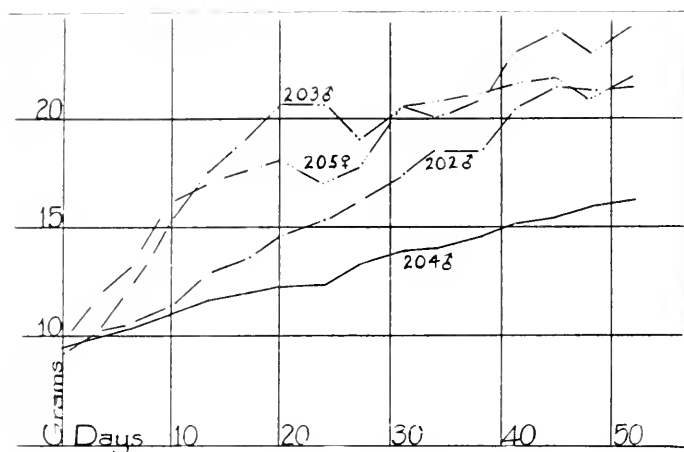


Chart 1.—Growth of four mice on Mellin's Food with varying amounts of milk added to the ration: Mouse 204 ♂ had Mellin's Food without milk; Mouse 202 ♂ had 1 c.c. of milk mixed with the day's ration; Mouse 203 ♂ had 3 c.c., and Mouse 205 ♀, 5 c.c. of milk. All had always an excess of food in the cage.

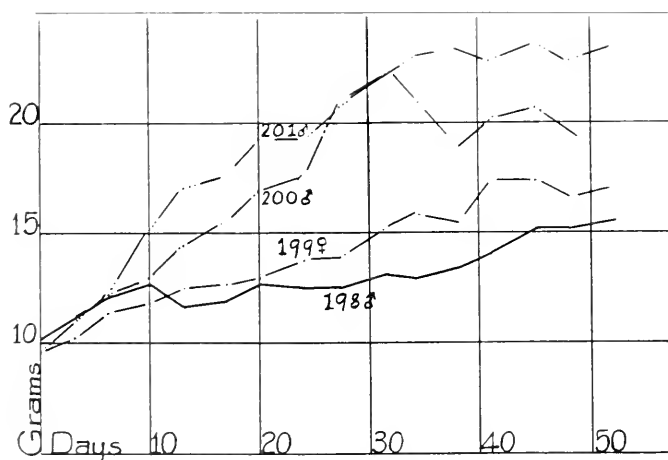


Chart 2.—Growth of four mice on Mellin's Food with varying proportions of milk added: Mouse 198 ♂ had no milk; Mouse 199 ♀ had 1 c.c.; Mouse 200 ♂ had 3 c.c., and Mouse 201 ♂, 5 c.c. of milk added to the day's ration. All had always an excess of food in the cage. The effect of 1 c.c. of milk is less evident than in the preceding chart because Mouse 199, a female, would normally grow more slowly than Mouse 198, a male.

was also a noon feeding, but as food given at this time was seldom touched, this feeding was omitted in the later series. Any mixture containing milk was kept on ice until put into the cages, and all containers were sterilized by boiling every time they were used.

Previous work had shown that the two food powders needed somewhat different treatment, Eskay's Food requiring the boiling recommended by the manufacturers. As far as the amount of milk allowed, both were fed as a thin paste as in the earlier work. When small proportions of milk were used, the food powder was mixed first with distilled water to a thick paste, then the milk was added from a pipette or a graduate and very thoroughly stirred in. With the larger proportions of milk, no water was used. Except with the largest amounts of milk, the physical consistency of the final mixtures was practically the same throughout and similar to that adopted in earlier work.

Both Mellin's Food and Eskay's Food had to be modified before they could be fed with small proportions of milk, both of them containing too little protein for mice, and Eskay's needing also an increased salt content. As in earlier work, the protein added was purified casein and the salt mixture, Osborne and Mendel's "protein-free milk." Both of these had been satisfactorily used before in long-continued experiments, both as the sole source of protein and of salts, respectively, and as modifiers of infant-foods, so that no unsatisfactory results can be attributed to them. With increasing proportions of milk, less added casein and protein-free milk were needed. Some of the mixtures contained unmodified foods mixed with the milk. Both the formulas for mixing and the composition of the final mixtures will be found in Tables 1 and 2.

TABLE 1.—FORMULAS AND COMPOSITION OF MELLIN'S FOOD MIXTURES

| Formula— | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|-----------------------|-----|-------|--------|--------|--------|---------|-----|--------|
| Mellin's Food | 93% | 93% | 93% | 93% | 93% | 93% | 90% | 90% |
| Casein | 7% | 7% | 7% | 7% | 7% | 7% | 7% | 7% |
| Olive oil | 0 | 0 | 0 | 0 | 0 | 0 | 3% | 3% |
| Milk to 4 gm. food... | | 1 cc. | 2 c.c. | 3 c.c. | 5 c.c. | 10 c.c. | | 1 c.c. |

COMPOSITION IN TERMS OF TOTAL SOLIDS

| | | | | | | | | |
|---|-------|-------|-------|-------|-------|-------|-------|-------|
| Protein | 18.3% | 18.6% | 19.2% | 19.5% | 19.8% | 20.8% | 17.7% | 18.3% |
| Ash | 3.6% | 3.7% | 3.7% | 3.7% | 3.7% | 4.2% | 3.5% | 4.2% |
| Fat | 0.7% | 1.6% | 2.5% | 3.4% | 4.8% | 8.0% | 3.6% | 4.5% |
| Carbohydrate | 77.4% | 76.1% | 74.6% | 73.4% | 71.7% | 67.0% | 73.2% | 72.9% |
| Calories to 100 gm. (computed) | 398 | 413 | 408 | 411 | 421 | 435 | 408 | 416 |

TABLE 2.—FORMULAS AND COMPOSITION OF ESKAY'S FOOD MIXTURE

| Formula— | 1 | 2 | 3 | 4 | 5 | 6 |
|-------------------------------|--------|--------|---------|---------|---------|---------|
| Eskay's Albuminized Food | 67% | 67% | 73% | 73% | 100% | 100% |
| Casein | 13% | 13% | 11% | 11% | | |
| Protein-free milk | 18% | 18% | 16% | 16% | | |
| Olive oil | 2% | 2% | | | | |
| Milk to 4 gm. food..... | 3 c.c. | 5 c.c. | 10 c.c. | 20 c.c. | 40 c.c. | 50 c.c. |

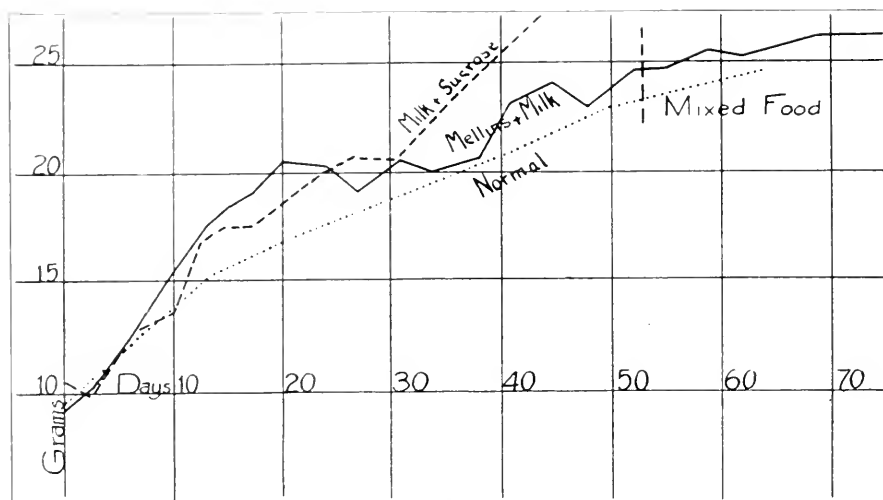


Chart 3.—Comparative growth of Mouse 203 ♂ (repeated from Chart 1) on Mellin's Food plus 2 c.c. of milk to the day's ration (4 gm.) and of Mouse 197 ♀ on milk plus 6.5 per cent. of sucrose. The dotted line indicates normal growth for mice.

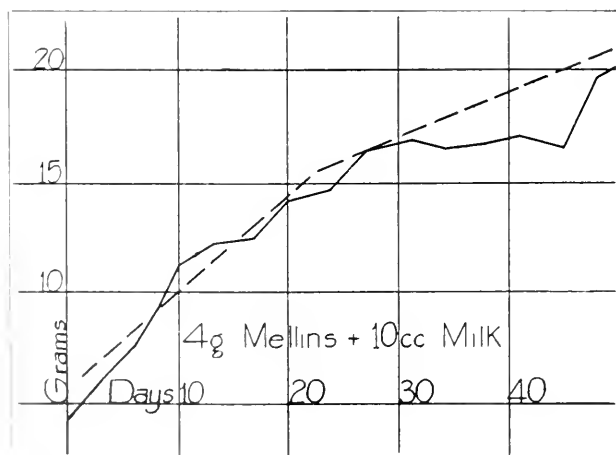


Chart 4.—Growth of Mouse 196 ♂ on Mellin's Food plus 10 c.c. of milk to the daily ration. The interrupted line shows normal growth.

COMPOSITION IN TERMS OF TOTAL SOLIDS

| Formula— | 1 | 2 | 3 | 4 | 5 | 6 |
|---|-------|-------|-------|-------|-------|-------|
| Protein | 19.2% | 20.0% | 18.5% | 21.7% | 18.7% | 21.2% |
| Ash | 3.8% | 3.9% | 3.8% | 4.2% | 3.8% | 3.7% |
| Fat | 5.3% | 6.8% | 5.1% | 12.6% | 16.9% | 19.2% |
| Carbohydrate | 71.7% | 69.2% | 72.7% | 61.5% | 60.7% | 55.9% |
| Calories to 100 gm. (computed) | 408 | 428 | 421 | 448 | 483 | 495 |

The effect of possible variations in the composition or in the bacterial content of the milk was watched by feeding, to at least one animal in each group, milk modified only by the addition of 6.5 per cent. granulated sugar. This mixture had a composition similar to that of the other foods. (See Table 3.)

TABLE 3.—COMPOSITION OF MILK AND SUCROSE MIXTURE

MILK + 6.5 PER CENT. SUCROSE. COMPOSITION IN TERMS OF TOTAL SOLIDS

| | % |
|--------------------------------------|------|
| Protein | 18.2 |
| Ash | 3.7 |
| Fat | 19.2 |
| Carbohydrate | 58.8 |
| Calories to 100 gm. (computed) | 508 |

MELLIN'S FOOD

In the earlier investigation, it was found that Mellin's Food unmodified could not serve as an exclusive ration either for young or for adult mice. The animals on such a diet steadily lost weight and eventually died unless the food was changed. Since other foods of closely similar gross composition served perfectly for maintenance through long periods, the difficulty could not lie in the percentage of protein, etc. It might, however, lie in either of two factors, namely, lack of essential accessory substances such as "vitamines" or "growth hormones," or in an inadequate supply from its proteins of essential amino-acids. Osborne and Mendel³ have recently shown conclusively that lysin is necessary for growth, and in two of the chief proteins of the grains from which Mellin's Food is manufactured, hordein of barley and gliadin of wheat, lysin is absent or present only in traces. The addition of 1 c.c. fresh milk per day to the diet of each mouse on unmodified Mellin's⁴ Food did not stop the decline in weight, so the trouble was not all in the lack of accessory substances. Five per cent. casein added to the ration, stopped the decline and allowed the lost weight to be regained as rapidly as on a general mixed diet;⁵ but no

3. Osborne and Mendel: Jour. Biol. Chem., 1914, 325.

4. Wheeler and Biester: AM. JOUR. DIS. CHILD., March, 1914, Chart 19.

5. Wheeler and Biester: AM. JOUR. DIS. CHILD., March, 1914, Chart 18.

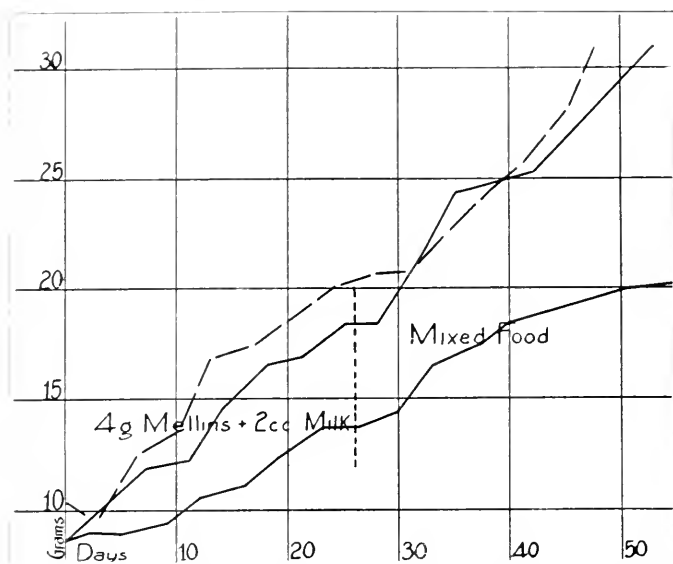


Chart 5.—Growth of two mice, Nos. 217 ♀ and 209 ♂ on a diet of Mellin's Food with 2 c.c. of milk added to each day's ration. For comparison the growth of a control animal 197 ♀ on milk plus 6.5 per cent. sucrose is shown in the interrupted line.

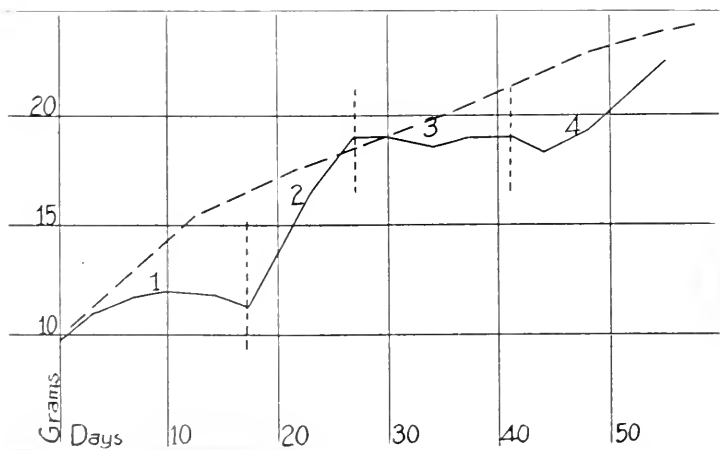


Chart 6.—Mouse 194 ♂, showing maintenance but no growth on a Mellin's Food-oil-casein food (periods 1 and 3) and rapid growth when to the day's ration of this food was added 1 c.c. of fresh milk. The interrupted line shows normal growth for mice. For the composition of the food, see Table 1, Formula 7.

further significant increase took place. There was practically no growth. The casein was able to supply the lack partially, but not completely.

In the present series of experiments a number of modifications of Mellin's Food were made. The composition of the most significant of them is given in Table 1, and some of the results of feeding them in Charts 1 to 6, inclusive. In each group of feeding trials, a single litter of mice was used. One or two animals were given the basal ration; for example, 93 per cent. Mellin's Food and 7 per cent. casein; a second group was given this plus 1 c.c. fresh milk to the day's ration; a third group 3 c.c., a fourth 5 c.c., and so on. The gross composition (in protein, salts and total energy value) of these diets did not vary outside the limits found to give normal growth in mice.

The mice receiving no milk grew only very slowly (see the solid line in Charts 1 and 2), although their food was practically identical in gross composition with a food on which normal growth and reproduction had occurred.⁶ The addition of 1 c.c. of milk to the day's ration of each mouse increased the growth rate decidedly (Charts 1 and 2 in this paper). The addition of milk made a food adequate to support entirely normal growth in mice, as is indicated in Chart 3. Later, a mixture of 2 c.c. milk and the same food (Mellin's, 93 per cent.; casein, 7 per cent.) was fed to two mice. One mouse grew at a normal rate (Chart 5); the other was evidently a sick animal, since a change to a general mixed diet did not materially affect the rate of gain in weight.

The effect of small quantities of milk on growth was still more clearly indicated in the reaction of mouse 194, which was fed a Mellin-casein-olive-oil mixture (Formula 7, Table 1, this paper) to see whether increasing the total energy value of the ration would hasten growth. The animal remained at nearly constant weight for seventeen days. Then 1 c.c. of milk was daily mixed with the food and the animal grew very rapidly, reaching normal weight for its age in ten days (Chart 6). On the withdrawal of milk from its dietary, all growth ceased at once, to be resumed almost immediately when 1 c.c. milk was again fed.⁷

6. Column 2, Food B, Table 172, previous paper.

7. Cf. Hopkins, F. G.: *Jour. Physiol.*, 1912, xliv, 425. Hopkins, working with rats, found that milk to the extent of 4 per cent. of the total solids of the food must be added to mixtures of isolated food substances (casein as the protein) in order to secure normal growth. In the present experiments, milk provided 5.8 per cent. or more of the total solids of growth foods.

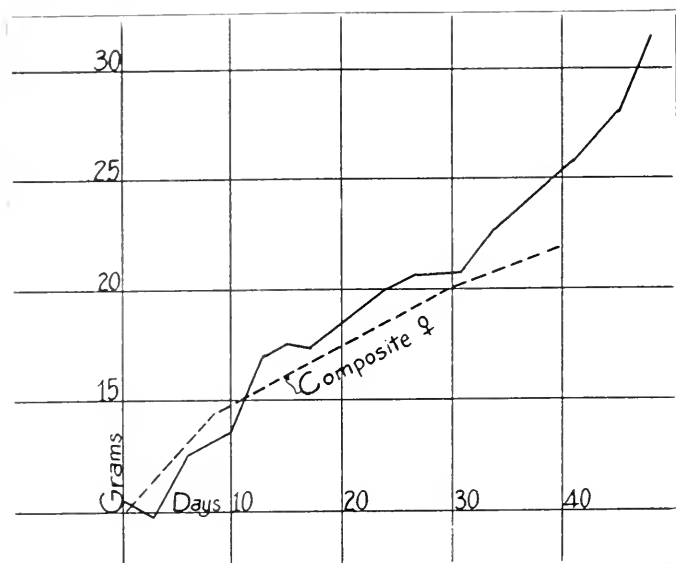


Chart 7.—Growth of Mouse 197 ♀ on a diet of fresh milk plus 6.5 per cent. sucrose. As is seen in the chart, the growth was more rapid than the "normal," which is indicated in the interrupted line.

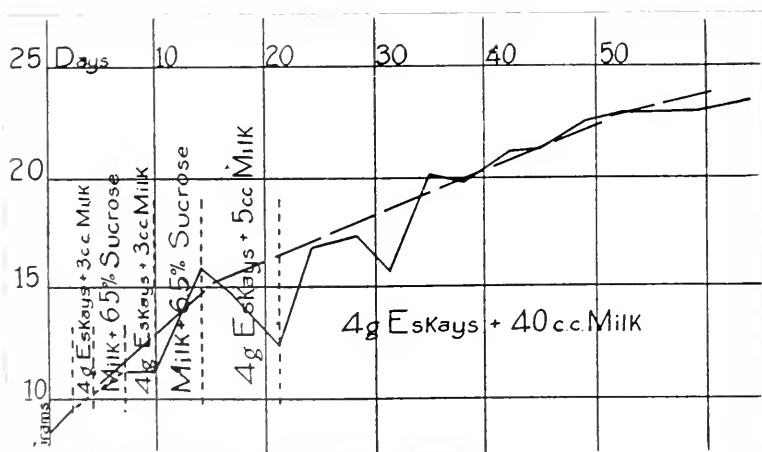


Chart 8.—Mouse 241 ♂, showing cessation of growth during the periods in which Eskay's plus small quantities (3 or 5 c.c. to the day's ration) of milk were fed and rapid growth when for this diet, milk plus 6.5 per cent. sucrose was substituted. The line is dotted during the second and third periods, because the mouse was so feeble at the end of two days' feeding with 4 gm. of Eskay's plus 3 c.c. of milk that the diet was changed without weighing the mouse.

CONCLUSIONS FROM FEEDING TRIALS WITH MELLIN'S FOOD

It would appear from these results that the reasons why Mellin's Food does not in itself satisfy all the nutritive requirements of maintenance and growth are (1) an inadequacy in its proteins and (2) a lack of some essential accessory substance. The inadequacy of its proteins is inferred from these facts: (a) fed unmodified as an exclusive ration, it does not support even maintenance, although other foods containing the same percentage of protein are entirely adequate for both maintenance and growth; (b) the addition of 5 per cent. or more casein to the food results in a regaining of the lost weight and continued maintenance. The improvement noted is due to the casein itself, not to an admixture in it of accessory substances, for 1 to 2 c.c. of milk daily, though furnishing "vitamines" in sufficient amount, had

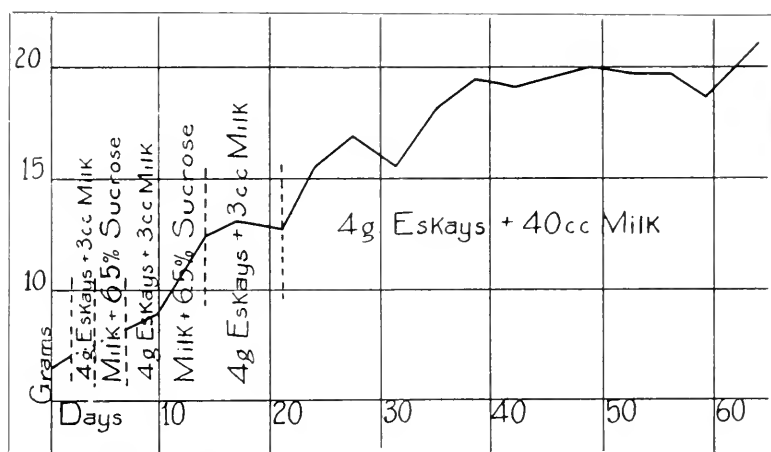


Chart 9.—Mouse 246 ♀, showing cessation of growth during periods in which Eskay's was fed with small quantities of milk and growth during periods in which the diet was either milk plus 6.5 per cent. sucrose or 4 gm. Eskay's plus 40 c.c. of milk. The graph is dotted through the first two periods because the mouse was so feeble at the end of the second day of feeding with the mixture of 4 gm. Eskay's plus 3 c.c. of milk that it was not weighed before the change of diet.

no effect in stopping the decline resulting from a diet of unmodified Mellin's Food.⁵ In the second place, it would appear that the lack of growth on Mellin's Food is due to the absence from it of some essential accessory substance, vitamine or growth hormone, for (1) practically no growth took place on the Mellin's Food-casein mixture, and (2) the addition of even 1 c.c. of milk to this last-named ration, although it added only 2.8 per cent. of nutrients, resulted in a great increase in the rate of growth. Nevertheless, Mellin's Food is some-

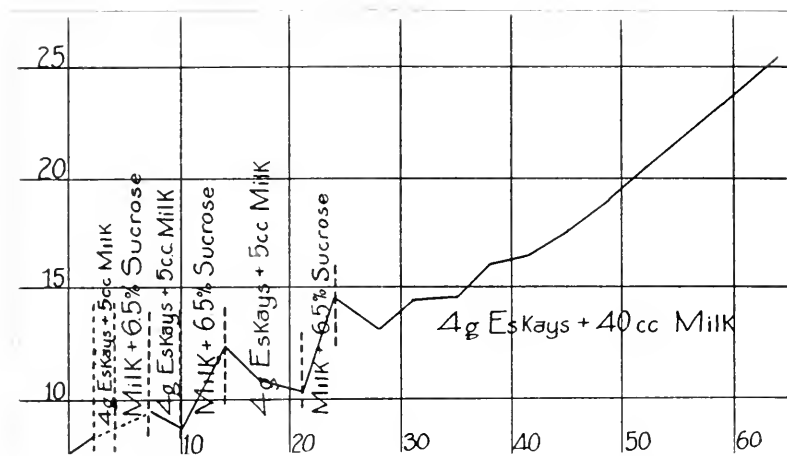


Chart 10.—Mouse 243 ♀, showing loss of weight during periods during which the diet was Eskay's Food plus small amounts of milk, and rapid gains in periods in which milk plus 6.5 per cent. sucrose was fed. Four gm. of Eskay's plus 40 c.c. of milk in the final period sustained a normal rate of growth.

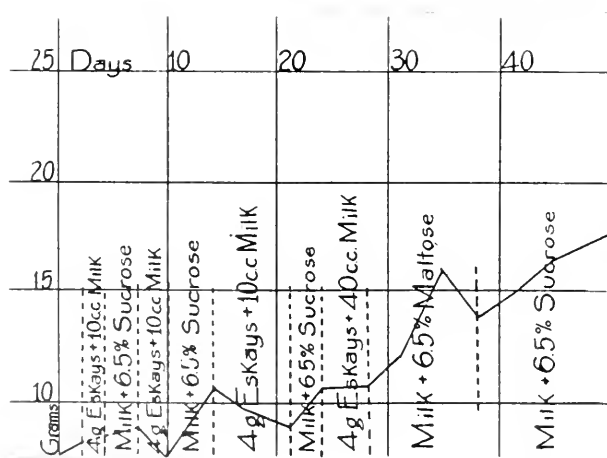


Chart 11.—Mouse 242 ♂, showing alternate gains in weight on a diet of milk plus 6.5 per cent. sucrose or maltose and loss of weight on Eskay's Food plus 10 c.c. of milk to the usual daily ration of solid food, 4 gm.

thing more than simply a milk modifier, for it may furnish nearly 90 per cent. of the total nutrients of a growth ration.

The control mouse receiving milk plus 6.5 per cent. sucrose grew quite as rapidly as did the animals on Mellin's and milk mixtures (see Charts 3 and 7).

ESKAY'S ALBUMINIZED FOOD

In feeding Eskay's Food with milk, the plan followed was much the same as that outlined for Mellin's Food. To 4 gm. of the food powder, varying amounts of milk were added, beginning with a minimum of 3 c.c. Preliminary feedings suggested the need of a high

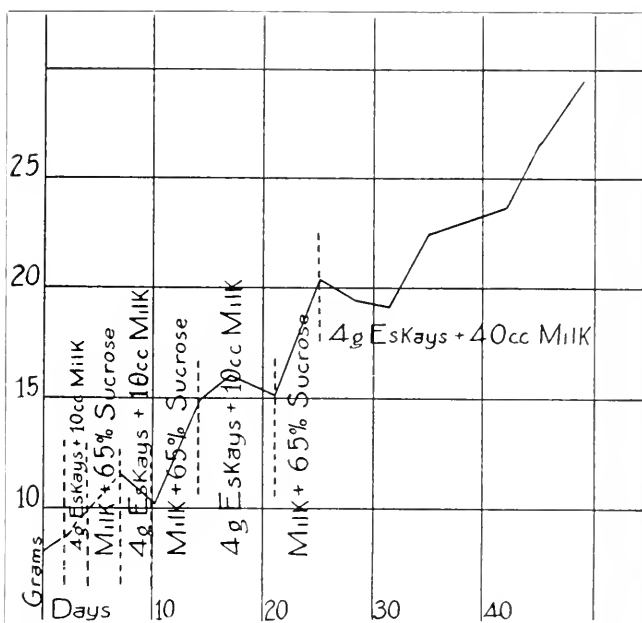


Chart 12.—Mouse 235 ♀, showing gains of weight in periods of feeding with milk plus 6.5 per cent. sucrose alternating with loss or simply maintenance in periods of feeding with a mixture of 4 gm. of Eskay's plus 10 c.c. of milk. The graph is dotted in the first and second periods because the mouse was so feeble after two days' feeding with the mixture of 4 gm. of Eskay's plus 10 c.c. of milk that its diet was changed without preliminary weighing.

maximum, and eventually 50 c.c. to 4 gm. of Eskay's was adopted. It was of course necessary to keep the gross composition of the final food mixtures within the limits possible in an exclusive diet for mice and also to make the different mixtures comparable in gross composition. This necessitated using unmodified Eskay's Food with the larger proportions of milk, and with the smaller proportions, adding to the food sufficient casein and salts (Osborne and Mendel's protein-free milk) to

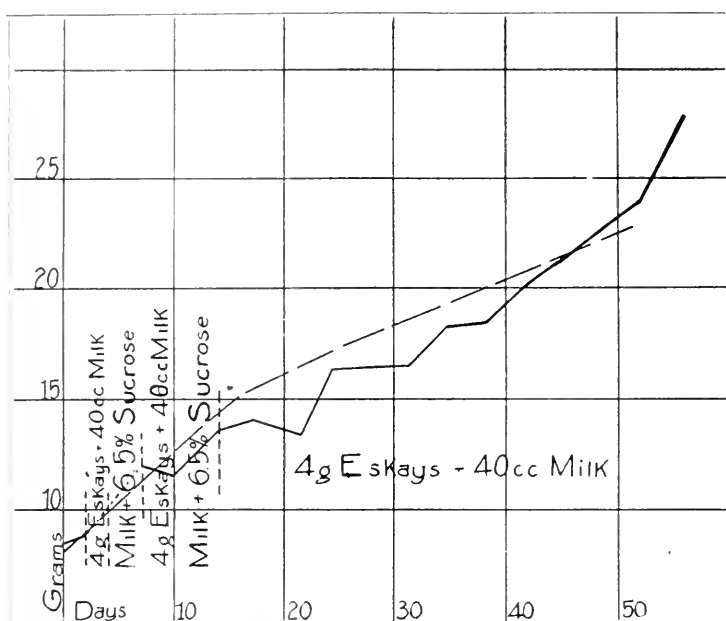


Chart 13.—Mouse 236 ♀, showing growth on a diet of milk plus 6.5 per cent. sucrose and cessation of growth on a diet of Eskay's Food plus 40 c.c. of milk to the usual daily ration (4 gm.). At the end of the first period on the Eskay's-milk mixture, the mouse was so feeble that its diet was changed without preliminary weighing of the animal. It is on this account that the graph is dotted in this and the following period. In the final period this same diet sustained normal growth.

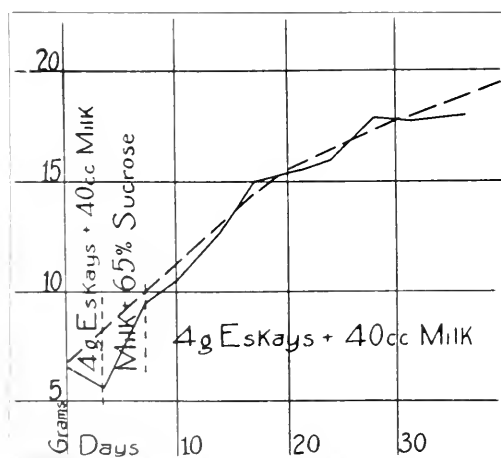


Chart 14.—Mouse 254 ♂, showing normal growth on a mixture of 4 gm. of Eskay's Food and 40 c.c. of milk after an initial loss on this same diet. The interrupted line indicates normal growth for mice.

enrich its protein and salts content. The modifications will be found in Table 2, this paper. It will be noticed that the final food mixtures, after the addition of milk in the proportions indicated in the formulae, are closely similar in gross composition. Slowness of growth cannot be attributed to the presence in food mixtures of casein or of protein-free milk, as both these have been used scores of times in food mixtures which sustained normal growth and reproduction. Since both the gross composition and the substances added have alike proved to be altogether satisfactory in growth foods, failure to grow in these trials must be due to some inadequacy in the nutrients present in the Eskay's Food, or to the absence from it of accessory substances, or to both these factors.

Unlike Mellin's Food, Eskay's must be boiled, as preliminary experiments showed. To every 10 gm. of the food powder, modified or unmodified as the case might be, a few cubic centimeters of distilled water was added to make a thin, smooth paste, the rest of 50 c.c. of distilled water added with constant stirring; the whole heated to boiling, still with constant stirring, and finally heated over boiling water, in a double boiler, for forty minutes. After rapid cooling in a stream of running water and replacing the evaporated water, the milk was thoroughly stirred in.

The previous experiments showed that Eskay's Food, modified to the proper gross composition and fed in a paste with distilled water, was insufficient to induce growth in young mice, or even, except in a single instance, to sustain life for any length of time. Boiling the food did not alter these results. With 3, 5 or 10 c.c. of milk added to the day's ration (4 gm.) the result was the same: very young animals lost weight rapidly, the first group of ten becoming so feeble by the second morning — forty-eight hours' feeding — that their diet was changed without even weighing them. On fresh cow's milk plus 6.5 per cent. sucrose,⁸ they rapidly recovered, weighing at the end of two more days from 30 to 60 per cent. more than at the beginning of the experimental feedings (see Charts 7 to 12, inclusive). On a return to the Eskay's-milk diets for the three succeeding days, all the animals either lost weight or just held their own; but though in most cases the relative loss of weight was not serious, the animals were all so evidently ill — with very rough coats, bodies hunched up, hind legs almost useless, and stools diarrheal — that all were again given the sucrose-milk diet for four days, during which very great gains in weight were made, the diarrhea disappeared completely, and the whole appearance of the animals became normal. The Eskay's-milk mixtures were then fed

8. This makes the protein 18 per cent. of the total solids of the food and the salt content 3.8 per cent.; i. e., comparable with that of the other foods.

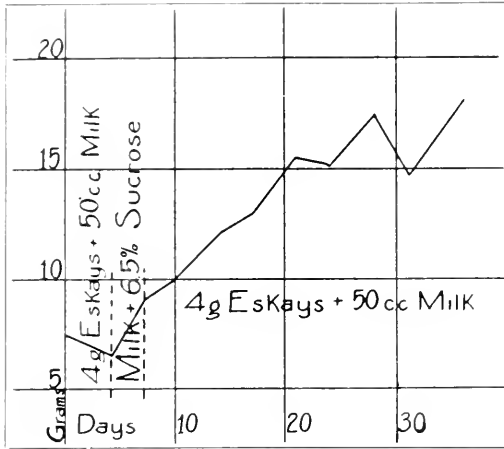


Chart 15.—Mouse 253 ♀, showing normal gain in weight on a mixture of 4 gm. of Eskay's Food and 50 c.c. of milk after an initial loss on this diet, and recovery on a milk-sucrose food.

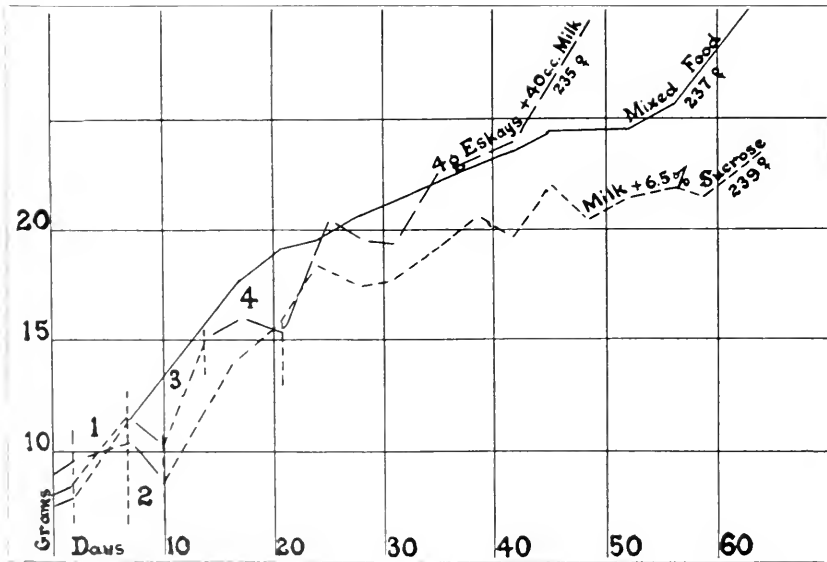


Chart 16.—Comparative growth on three dietaries: mixed food, milk plus 6.5 per cent. sucrose and 4 gm. of Eskay's Food plus 40 c.c. of milk. The last section of the highest line represents a pregnancy curve (Mouse 235 ♀). For diets during the first twenty days see Charts 12 and 17.

once more, this time for a week, with results similar to those in the preceding periods on these diets, but the symptoms of disturbance generally were less marked. The larger animals showed the effects less quickly. Then the whole group of animals was given a mixture of 40 c.c. of milk to 4 gm. of Eskay's,⁹ the latter used now without modification, as so large a proportion of milk furnished enough protein and salts to make the resulting mixture of the right composition (see Formula 5, Table 2, this paper). The rate of growth for the succeeding thirty days compared favorably with that of the controls from the same litters on a general mixed diet and with that of two other controls on the milk-sucrose food. During this period there was a tendency to diarrhea on the part of a few of the mice on an Eskay-milk diet, but not continuously or in all the animals. Chart 14 also shows growth on this same mixture and Chart 15, growth for a considerable period on a mixture of 50 c.c. of milk with 4 gm. of Eskay's Food.

REPRODUCTION

Two female mice, 235 and 236, on a ration of Eskay's Food and milk in the proportion of 40 c.c. milk to 4 gm. Eskay's Food, became pregnant, bore and reared the young. Mouse 235 had had the diet twenty-five days and mouse 236 forty-three days before the birth of the young. The litters were numerically small in both cases, two mice in one litter and four in the other, as compared with from eight to twelve in litters of animals on a general mixed diet; but nevertheless, the successful rearing of the young to normal size at the end of the nursing period, is significant evidence that the food mixture in question contained the substances necessary for growth in mice.

CONCLUSIONS FROM FEEDING TRIALS WITH ESKAY'S ALBUMINIZED FOOD

Eskay's Albuminized Food, used strictly as a milk modifier, allows normal growth in mice. In the most satisfactory mixture studied, Eskay's Food furnished 6.1 per cent. of the ration as fed, or 33 per cent. of the actual nutrients (total solids). Milk must furnish more than half the total nutrients if there is to be normal growth.

The absence of growth in animals in whose diet Eskay's Food forms 60 per cent. of the total nutrients, indicates that the character of the nutrients is at fault — that the difficulty is not due simply to the lack of essential accessory food substances. That these last-named essential substances are lacking, however, seemed indicated in the earlier series of feeding trials in which mice showed only minimal

9. This formula closely resembles that recommended by the manufacturers for a child six months old.

growth on a mixture of Eskay's Food with casein and milk salts ("protein-free milk") in which over 95 per cent. of the protein and the same proportion (95 per cent.) of the salts were purified milk products.

In Chart 16 an attempt has been made to summarize the results of these experiments. The cessation of the growth or actual decline on foods in which Eskay's Food furnished 50 per cent. or more of the nutrients is shown in the sections of the graph marked 2 and 4, between vertical dotted lines. The rapid gain in weight when the diet was changed to milk containing 6.5 per cent. sucrose is shown in sections of the graph marked 1 and 3. It will be noted that rapid gain in weight was also made on a ration of 4 gm. of Eskay's in 40 c.c. milk.

In this series also, granulated sugar proved quite as adequate a modifier of cow's milk as the prepared food, as far as the rate of growth and the apparent health of the animals is concerned.

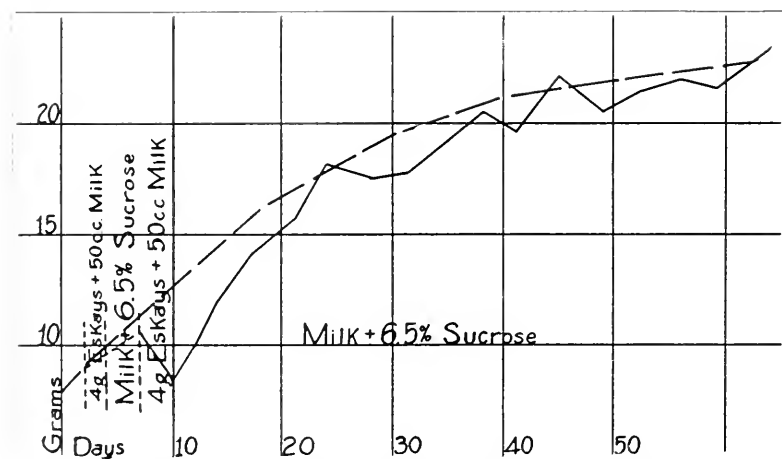


Chart 17.—Mouse 239 ♀, showing normal growth on milk plus 6.5 per cent. sucrose.

SUMMARY

Mixtures of milk and Eskay's Albuminized Food sustain normal growth in albino mice provided the milk furnishes 94 per cent. of the mixture as fed (66 per cent. of solid nutrients).

The lack of growth on Eskay's Food without milk appears to be due to two factors: (1) inadequacy of the proteins to satisfy the nutritive requirements for growth in mice, and (2) absence from this preparation of some accessory substance or substances essential to growth.

Eskay's Food in milk mixtures, as when fed without milk, produces in mice soft stools and sometimes diarrhea.

Mixtures of Mellin's Food and milk also sustain normal growth in mice. Here, too, the milk serves two purposes: to supplement inadequate proteins and to supply essential accessory food substances.

A mixture of 93 per cent. Mellin's Food and 7 per cent. purified casein is adequate for long-continued maintenance, but not for growth; 2 c.c. of milk added to the daily ration (4 gm.) of this mixture, makes a food which sustains entirely normal growth in mice. Here, milk furnishes 5.8 per cent. (including casein, 7.2 per cent.) of the total solids of the diet.

The feces of animals on a diet of Mellin's Food mixtures were always comparatively hard and dry.

A mixture of fresh milk and 6.5 per cent. sucrose also sustained entirely normal growth in young mice. From an economic standpoint at least, this fact deserves consideration.

STUDIES ON INFANT METABOLISM AND NUTRITION

UNDER THE DIRECTION OF L. EMMETT HOLT, M.D., AND
DONALD D. VAN SLYKE, PH.D.

*The Excretion by Infants of Magnesium Sulphate Injected Subcutaneously**

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AND
HELEN L. FALES
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Since Meltzer and Auer demonstrated the narcotic action of magnesium salts injected into the circulation, several clinical applications of this action have been found valuable.

For example, magnesium sulphate has been used intraspinally with excellent results to combat the convulsions of tetanus,¹ in many parts of the world.² Magnesium sulphate also induces an anesthesia which permits surgical intervention.³ It has recently been found that a combination of magnesium sulphate (subcutaneous) and ether (inhalation), produces a surgical anesthesia which is not obtained when either in the same amount is used alone.⁴ It may also be mentioned that saturated solutions of magnesium sulphate are employed for the local treatment of burns and erysipelas.

Recently, Behrend⁵ has utilized magnesium sulphate, injected subcutaneously into infants, to alleviate the convulsions of tetany. The salt proved remarkably effective in immediately stopping convulsions and reducing the condition of hyperirritability. As the effect was temporary, however, the injections had in the most severe cases to be repeated on a number of successive days. Because of this necessity it appears highly desirable to ascertain the rate at which magnesium sulphate is eliminated after subcutaneous injection. For if the doses require more than twenty-four hours for their excretion, daily repetition of the injection would lead to an accumulation of magnesium in

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* From the Chemical Laboratories of The Rockefeller Institute for Medical Research and The Babies' Hospital, New York.

1. Meltzer, S. J., and Auer, J.: Jour. Exper. Med., 1906, xiii, 692.

2. See for example, Rocher, Theodore (Cor.-Bl. f. schweiz. Aerzte, 1912, lxii, 969); Stadler, H. (Berl. klin. Wehnschr., 1914, li, 15; *ibid.*, 109); Weintraud, W. (*ibid.*, 1717).

3. Haubold, H. A., and Meltzer, S. J.: Jour. Am. Med. Assn., 1906, lxvi, 647.

4. Meltzer, S. J., and Auer, J.: Zentralbl. f. Physiol., 1914, xxvii, 632.

5. Behrend: Monatsch. f. Kinderh., 1913, xii, 269.

EXCRETION BY INFANTS OF MAGNESIUM SULPHATE INJECTED SUBCUTANEOUSLY

| Date | MgO Received | | | MgO Excreted | | | MgO Balance | Sulphate Injected (Calc. as H ₂ SO ₄) | Sulphate Excreted in Urine | Sulphate Excreted in Urine in excess of Injected Amount |
|---|--------------|----------|--------|--------------|--------|--------|-------------|--|----------------------------|---|
| | Food | Injected | Total | Feces | Urine | Total | | | | |
| David W.;* Weight, 5,799 gm.; Age, 5 months | | | | | | | | | | |
| 12/1 | 0.1186 | 0.2683 | 0.3869 | 0.0772 | 0.1403 | 0.2175 | +0.1694 | 0.6513 | 0.5166 | 0.1653 |
| 12/2 | 0.1156 | 0.1878 | 0.3034 | 0.0772 | 0.2603 | 0.3375 | -0.0341 | 0.4560 | 0.9895 | 0.5335 |
| 12/3 | 0.1258 | | 0.1258 | 0.0698 | 0.0178 | 0.0876 | +0.0382 | | 0.2387 | 0.2387 |
| 12/4 | 0.1216 | | 0.1216 | 0.0698 | 0.0266 | 0.0964 | +0.0252 | | 0.2273 | 0.2273 |
| 12/6 | 0.1016 | 0.2683 | 0.3699 | 0.0698 | 0.1616 | 0.2314 | +0.1385 | 0.6513 | 0.8165 | 0.1652 |
| 12/7 | 0.1198 | | 0.1198 | 0.0698 | 0.0237 | 0.0935 | +0.0263 | | 0.1760 | 0.1760 |
| Joe D.; Weight, 3,845 gm.; Age, 5 months | | | | | | | | | | |
| 12/1 | 0.0798 | 0.2683 | 0.3481 | 0.0658 | (lost) | | | 0.6513 | 0.9993 | 0.3480 |
| 12/2 | 0.1033 | 0.1342 | 0.2375 | 0.0658 | 0.0649 | 0.1307 | +0.1068 | 0.3257 | 0.5231 | 0.1974 |
| 12/3 | 0.1028 | | 0.1028 | 0.0658 | 0.0224 | 0.0882 | +0.0146 | | 0.1717 | 0.1717 |
| 12/4 | 0.1033 | | 0.1033 | 0.0658 | 0.0065 | 0.0723 | +0.0310 | | 0.2132 | 0.2132 |
| 12/5 | 0.1033 | | 0.1033 | 0.0707 | 0.0134 | 0.0841 | +0.0192 | | 0.2206 | 0.2206 |
| 12/8-11 (per day) | 0.1110 | | 0.1110 | 0.0840 | | | | | | |
| Peter L.; Weight, 9,568 gm.; Age, 10 months | | | | | | | | | | |
| 2/2 | 0.1940 | 0.1073 | 0.3013 | 0.1165 | 0.0698 | 0.1863 | +0.1150 | 0.2605 | 0.7006 | 0.4401 |
| 2/3 | 0.1925 | 0.2146 | 0.4071 | 0.1165 | 0.2093 | 0.3258 | +0.0813 | 0.5211 | 1.1455 | 0.6244 |
| 2/4 | 0.1940 | | 0.1940 | 0.1165 | 0.0690 | 0.1855 | +0.0085 | | 0.4754 | 0.4754 |
| 2/5 | 0.1940 | | 0.1940 | 0.1608 | 0.0464 | 0.2072 | -0.0132 | | 0.3424 | 0.3424 |
| 2/6 | 0.1940 | | 0.1940 | 0.1608 | 0.0455 | 0.2063 | -0.0123 | | 0.5067 | 0.5067 |
| Elvira P.; Weight, 3,720 gm.; Age 3½ months | | | | | | | | | | |
| 10/ 9-10 | 0.100 | | 0.100 | | | 0.0767 | +0.0233 | | 0.1443 | |
| 10/10-11 | 0.070 | | 0.070 | | | 0.0426 | +0.0274 | | 0.1127 | |
| 10/11-12, 1st 12 hrs. | | | | | | 0.0792 | | | 0.2427 | |
| 10/11-12, 2d 12 hrs. | | | | | | 0.0408 | | | 0.1042 | |
| 10/11-12, altogether | 0.085 | 0.100 | 0.185 | | | 0.1200 | +0.0650 | 0.2451 | 0.3469 | 0.1018 |
| 10/12-13, 1st 12 hrs. | | | | | | 0.1330 | | | 0.1897 | |
| 10/12-13, 2d 12 hrs. | | | | | | 0.0814 | | | 0.1371 | |
| 10/12-13, altogether | 0.080 | 0.200 | 0.280 | | | 0.2144 | +0.0656 | 0.4902 | 0.6268 | 0.1366 |
| 10/13-14 | 0.100 | | 0.100 | | | 0.1126 | -0.0126 | | 0.0934 | |

* In this patient the injections of Dec. 1 and 2 were made 9 hours after the beginning of the 24-hour metabolism periods.

the body. Such an accumulation, in view of the toxicity of magnesium salts, could not be regarded without apprehension.

We have recently had occasion to use magnesium sulphate, in the manner described by Behrend, in treating a number of cases of tetany. The clinical effects were identical with those described by him. The irritability was immediately reduced, and did not return for the greater part of twenty-four hours. Some infants with especially severe convulsions were greatly benefited by the injections. In three cases we have followed the magnesium and sulphuric acid metabolism on the days succeeding the injections. The data are not so full as could be desired, as regards either the number of cases or the number of successive injections received by the individual patients. They are published, however, as they are the only observations available on the question, and the opportunities for obtaining more data are, from the nature of the problem, somewhat uncertain.

The magnesium sulphate was in each case injected subcutaneously with a syringe into the cellular tissue of the abdomen. The concentration of the solutions was 8 gm. of anhydrous MgSO_4 (equivalent to 16.4 gm. of Epsom salts) per 100 c.c., the volumes injected varying from 4 to 10 c.c. The children were placed in a comfortable metabolism bed which permitted the collection of urine and feces separately, and the excreta during the succeeding days were analyzed for magnesium and sulphates. The magnesium content of the food was also determined, so that the magnesium balance could be ascertained. The presence of organic sulphur in the food proteins makes a determination of sulphate balance impossible. We can, however, compare the daily excretion of sulphates when no magnesium sulphate is injected, with the excretion in the periods following the injections, and from the increase in these periods decide whether the injected SO_4 is excreted, and the rapidity with which the excretion occurs.

The results indicate the following:

MAGNESIUM

The increase in the elimination of magnesium by the feces is not sufficiently marked to make it certain that an important part of the injected magnesium is eliminated in this way.

In the urine, on the contrary, an increased magnesium excretion immediately followed the injection and practically ceased within twenty-four hours. The relation of the amount excreted to that injected was rather peculiar. A portion of the magnesium given in the first injection was, in two of the three cases, retained. When on the following day, however, another injection was given, an amount equivalent to the second injection was eliminated within twenty-four

hours. In the second case (J. D.) elimination of the second injection was incomplete. In no case was there conclusive evidence that any of the retained magnesium underwent gradual elimination during the succeeding days. The magnesium balance became normal again on the day after the injection. The magnesium is excreted within a period of about twenty-four hours or some of it is permanently retained. In Case 4 a separate collection of the urine and feces was impossible; but the intake and the total excretion are included in the table. In this patient the excretion was measured in twelve-hour periods after the injection. These figures show that the greater part of the elimination occurs in the first twelve hours. The amount excreted was twice as great as in the second twelve-hour period. On the second day, with an injection of 0.2 gm., the retention was no greater than on the first day after an injection of 0.1 gm. During the second twenty-four hours following the last injection the excretion was about 0.04 more than with the same intake before the first injection. On this day, therefore, he disposed of about one-half of the extra amount retained during the days of injection.

In brief, although the data do not cover enough ground to be conclusive, they indicate that the infant organism can incorporate within two successive days as much as one- or two-tenths of a gram of magnesium oxid from the magnesium sulphate injected subcutaneously, and that amounts in excess of this are immediately excreted by the kidneys.

In the doses mentioned in this paper there appears therefore to be no danger of cumulative effect of magnesium if the dose is not repeated more frequently than once in twenty-four hours. The smaller dose referred to is calculated for an average infant of from one to four months and the latter for one from five to ten months. These are equivalent respectively to 0.6 gm. (10 grains) and 1.6 gm. (25 grains) of Epsom salts or one-half the amount of anhydrous magnesium sulphate. Marked physiologic symptoms are usually produced with this dosage and in many cases smaller doses will suffice.

SULPHATE

The injected SO_4 is immediately and completely excreted in the urine. In fact, as will be seen from the last column, the rise in sulphate excretion on the day of injection corresponded to even more than the amount injected in two cases (the second injection of D. W. and the first of J. D.). After the other five injections the rise in excretion approximately equaled the amount injected.

TUBERCULOSIS AS A DISEASE OF THE NEWBORN*

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It seems to us that of all the chapters in medicine the most neglected is that of diseases of the newborn. We are only beginning to get here and there a little light on the clinical pictures here presented, and this shows us that the newborn infant is affected clinically by the same infections in a much different way from the older infant. It is for this reason that we wish to call attention to the subject of tuberculosis in the newborn, with the hope, not of adding a great deal to the literature, but of stimulating interest in a subject which has been so long neglected.

Much has been said and written about tuberculosis in children, and not a little about congenital tuberculosis. This has been a field which has been much studied by pathologists, but in which, as yet, the clinician has taken little interest. This is probably due to two causes: (1) the hopelessness of the case should the diagnosis be made, and (2) the extreme difficulty of making the diagnosis.

Though recognizing these facts, we feel that an attempt to add something to the clinical picture of tuberculosis may eventually be of practical as well as of scientific interest.

E. R. entered Cook County Hospital, obstetrical ward, Aug. 30, 1912, aged 20 years. She was transferred from the obstetrical ward to the woman's venereal ward because of a leukorrhea which, though suspicious, yet contained no organism which could be positively identified as the gonococcus. So far as the history shows, examination was negative except for an old, apparently healed, tuberculosis of the hip. It might be stated here that she left the hospital in good health and was known to be in apparently good health for several months after leaving the hospital, a notable fact in this case.

September 6 she gave birth to a baby, weighing 6 pounds, 8 ounces. This child was of a fair degree of nutrition and apparently at term. The temperature curve is best shown in the accompanying chart (Fig. 1). It will be noted that from the second day on the child ran an irregular temperature, varying between 98.6 F. and 105 F. During the first night the baby was very cross, and continued in that state for several days. The child did not get much from the breast and often refused to take the bottle feeding. Aside from warm packs for temperature and an occasional enema, no treatment was given. At 8:40 a. m. on the 13th the child had its first convulsion. It had two more convulsions before noon of that day. At that time the child was seen by one of us and the general examination revealed a child in a fair state of nutrition, apparently unconscious, with facial twitchings and eyes turned upward, first to the one side and then to the other. There were no râles distinguishable in the lungs; the heart area was not increased, nor were any murmurs detected. The liver was about 2 inches below the costal margin in the right mammary

* Received for publication Jan. 30, 1915.

line. The spleen was palpable. There was no enlargement of the epitrochlear glands and no infection that could be detected of the umbilical vessels. Despite the latter fact, a tentative diagnosis of septic infection was made, the possibility of such a condition complicating congenital syphilis being considered. From this time the child was given albumin milk. It had to be fed with a medicine dropper and regurgitated most of what was given. No further convulsions were recorded until the evening of the same day, when four more convulsions occurred within an hour, and a fifth before midnight. The amount of food taken was very small, at times being only 1 or 2 drams. For the control of the convulsions 2 grains of chloral hydrate rectally were administered on the morning of the 15th. This was repeated again in the afternoon and again in the evening. After the administration of the chloral hydrate the convulsions became much fewer, but did not cease altogether until the evening of

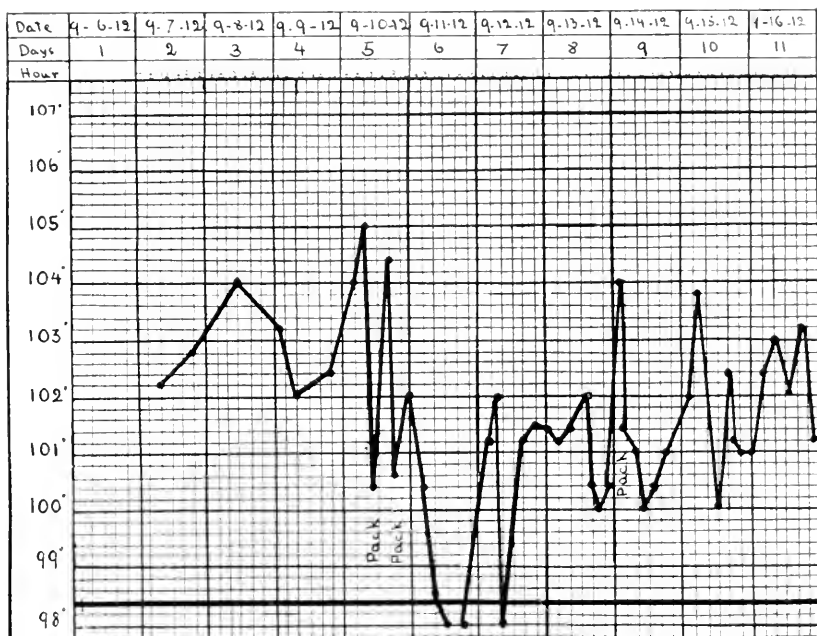


Fig. 1.—Temperature curve in tuberculosis of the newborn.

the 15th, after which time no further convulsions occurred. The child died at 11 p. m. on September 16. At necropsy the following was found:

Baby R., aged 11 days.

Body is that of an emaciated infant, about 50 cm. long, weighing about 7 pounds. Post-mortem lividity and rigor are not well marked. Eyes, ears and nose are negative. No marks of injury to head. Fontanelles large and gaping.

Brain: Congestion of superficial vessels over the right hemisphere. Cerebrospinal fluid increased slightly in amount. Cross sections of pons, cerebrum and medulla are negative. Ventricles are normal in size and contain a normal amount of fluid.

Thorax: Pleural cavities contain a small amount of clear, straw-colored fluid. Pericardium contains a small amount of a similar fluid. Pleura and pericardium are smooth and shiny.

Lungs: Collapse only slightly. Surface is uneven, showing depressions—irregular—and of a bluish color. Everywhere crepitant. Lungs are studded with a few scattered nodules, yellow-white in color, firm, up to size of sago seed. Cut surface: Moist, red and shows similar nodules, peribronchial thickenings. Peribronchial glands markedly enlarged (Fig. 2).

Heart: Normal size. Musculature reddish-brown. In wall of left ventricle is a small white nodule, size of a pinhead. Aortic, pulmonic, tricuspid, and mitral valves are normal.

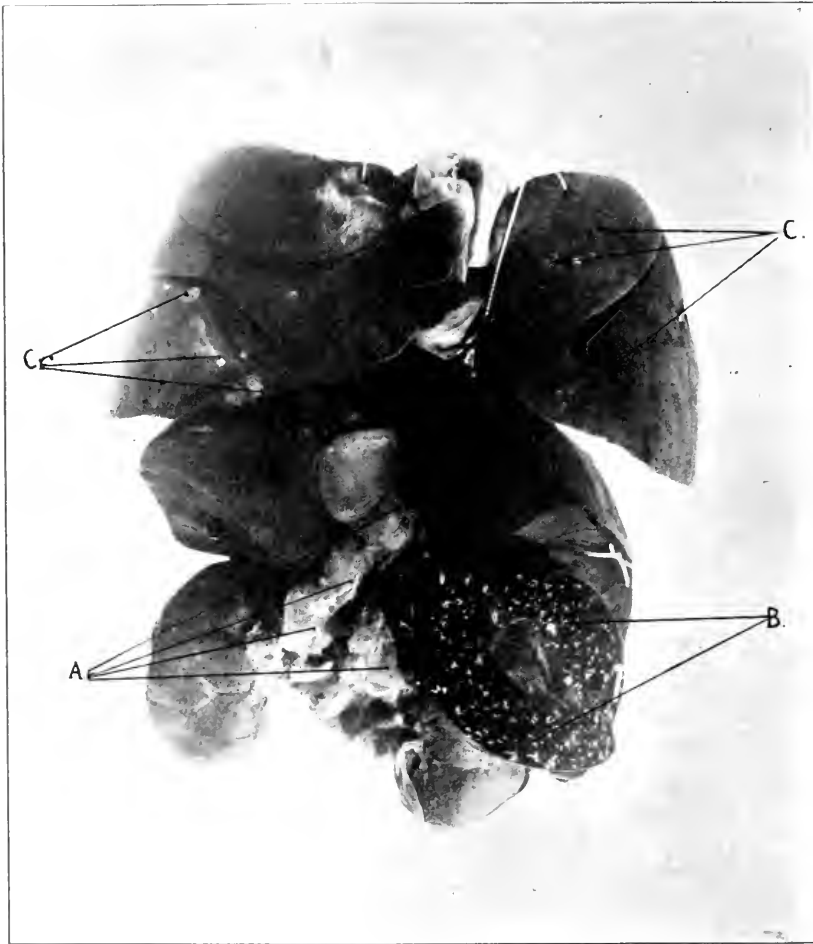


Fig. 2.—Tuberculosis of the newborn. *A*, tuberculous mesenteric and periportal glands. *B*, miliary tuberculosis of the spleen. *C*, tubercles in the lungs.

Abdomen: No free fluid. Peritoneum smooth and shiny. Ileocecal region is free. In region of gall-bladder is a massive growth, surrounding the gall passage, the size of a walnut, nodulated with masses up to size of a pea.

Liver: About normal size. Studded with a few nodules, both on the external and on the cut surface, similar to those described. Cut section: Lobules are very indistinct; parenchyma cloudy.

Pancreas: Head is imbedded in the mass surrounding the gall passage and is studded with similar nodules.

Spleen: Firm. Studded thickly with nodules up to size of sago seed (Fig. 2).

Kidneys: Fetal lobulation. Markings fairly distinct. A few nodules similar to those described.

Adrenals: Fairly large and show an occasional nodule.

Stomach: About normal size. Along lesser curvature are nodules up to size of small pea.

Intestines: Negative.

Mesenteric Glands: Enlarged, soft, red-gray. Microscopically, the nodules are seen to be made up of a coalescence of tubercles. A great number of tubercle bacilli are present.

Anatomic Diagnosis: Miliary tuberculosis of all organs, with tuberculosis of mesenteric lymph glands.

EPICRISIS

We have, then, the child born of a mother with supposedly a healed tuberculosis, whose only subjective symptom was a severe leukorrhea of unknown cause. The mother survived the child (an unusual thing in these cases) many months at least, and probably is still living. A baby born apparently at term and apparently healthy, had as early as fifteen hours after birth a high temperature, which continued irregularly until death. There was a distinct tendency to regurgitation, and on the seventh day generalized convulsions developed, which continued up to twenty-four hours before death. Death occurred on the eleventh day. On physical examination the child showed only an enlarged liver and enlarged spleen. At necropsy a generalized tuberculosis affecting most markedly the abdominal organs, and especially the periportal lymph-glands, liver and spleen was found. The tuberculosis was miliary in type, but the stage of the tubercles suggests that it had already begun *in utero*. Many tubercle bacilli were found in all sections of tuberculous areas (Fig. 3).

GENERAL CONSIDERATION

Tuberculosis of the placenta has been described by many authors. This is of importance in relation to tuberculosis of the fetus in proportion as the fetal or maternal portion of the placenta is involved. It is certain that in many cases only the maternal portion is involved, the fetal remaining uninfected by the tuberculous condition.

As to the relative frequency of tuberculosis of these two portions, it has been impossible for us to judge from the authorities consulted. It is worthy of note, however, that both placental tuberculosis and congenital tuberculosis are being reported with increasing frequency within the last few years.

The most exhaustive work on human congenital tuberculosis is that of Warthin and Cowie¹ published in 1904. They separate the authentic cases from those not sufficiently supported by evidence and find only five cases of certain congenital tuberculosis.

1. Warthin and Cowie: Jour. Infect. Dis., 1904, i, 140.

Cases of unquestioned tuberculous bacillosis have been reported by Bugge,² Londe³ (Case 5), Thiercelin and Londe,⁴ and Schmorl and Kockel.⁵ Nothing further need be said of this condition here except that it may form the basis for the development of cases of congenital tuberculosis which die after the first few weeks, if in fact such exist, about which there is a reasonable doubt.

Of the cases of tuberculosis of the newborn judged from a pathologic standpoint there are two forms, both of which of course are miliary in type: (1) pulmonary and (2) abdominal. (It should be stated here that all cases of this age reported as localized tuberculosis lack evidence necessary to be convincing.)

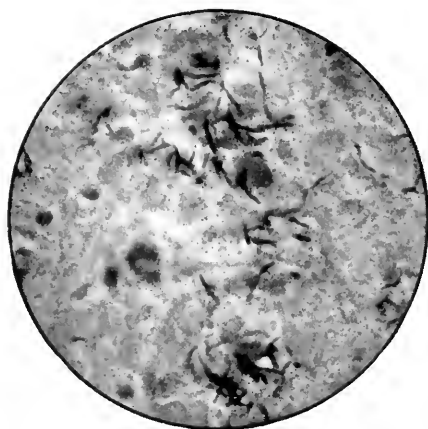


Fig. 3.—Showing tubercle bacilli in the liver tissue.

The first form is represented by the cases of Harbitz⁶ and Brindeau.⁷ In each of these the thoracic organs alone were affected and there was no involvement below the diaphragm. In the case of Harbitz the mother had an endometrial tuberculosis; in that of Brindeau no mention is made of the location of the tuberculosis in the mother. Brindeau's patient died on the twelfth day and showed large caseous nodules in the base of the lungs; Harbitz' patient died on the twenty-fifth day and showed miliary tuberculosis of the lungs with caseous peritracheal glands. There can be little doubt that the case of Brindeau is one of congenital tuberculosis. A doubt, however, may be raised as to that of Harbitz, because of the age to which the child lived, but

2. Bugge: *Beitr. z. path. Anat. u. z. allg. Path.*, 1896, xix, 433.

3. Londe: *Rev. de la Tuberc.*, 1893, i, 125.

4. Thiercelin and Londe: *Centralbl. f. Chir.*, 1894, xxi, 563.

5. Schmorl and Kockel: *Beit. z. path. Anat. u. z. allg. Path.*, 1894, xvi, 313.

6. Harbitz: *München. med. Wchnschr.*, 1913, ix, 741.

7. Brindeau: *Bull. Soc. d'Obst. de Paris*, 1899, ii, 235.

considering the presence of the endometrial tuberculosis it is altogether likely that the infection was congenital. In these cases one must look for a port of entry for the infection other than the umbilical vessels. In other words, placental infection need not be regarded as essential to this form. Much more likely would seem to be an aspiration of infected liquor amnii or vaginal secretions at the time of birth. While this might account for the location of the infection in the infant it would not coincide with the advanced nature of the lesion such as is seen in the case of Brindeau or perhaps in that of Harbitz. From the stage of the lesions it is altogether likely that the infection occurred *in utero*. If this be true, then the only plausible explanation is that it is due to an infection of the liquor amnii, an infection which might readily take place with an endometrial tuberculosis as in the case of Harbitz. There are two objections to this theory; the first is that the fetus is not supposed to respire *in utero* and hence the infected liquor amnii would not come in contact with the alveoli so as to produce lesions in the lungs. To explain the case of Harbitz it is only necessary to recall the recent work of Ghon,⁸ Wollstein and Bartlett,⁹ and others, which goes to show that the primary lesion may be in the bronchi (which are exposed to the liquor amnii) from which the neighboring lymph glands about the hilum are infected, and from these the lesion extends to the rest of the lung. Such an explanation, however, will not hold for the case of Brindeau. If we accept the recent work of Addison and How¹⁰ and of Ridella¹¹ it is altogether likely that the infant does respire *in utero*, in which case the infection of the deeper portions of the lungs would be readily explained. The other objection is that in both these cases the intestines have remained free. It is a well-known fact that the intestinal mucosa in extra-uterine life is quite resistant to tuberculous infection and it is quite likely that such is the case *in utero*, especially when we take into consideration that in its parasitic state the fetus does not use the intestinal canal for the purpose of supplying nutriment to the body.

The second or abdominal form might be termed the general miliary form. While the lesions are more marked in the abdominal cavity the thoracic viscera are always involved. We have been able to find in the literature ten cases of this form of tuberculosis¹² of the newborn other

8. Ghon: Der primäre Lungenherd bei der Tuberkulose der Kinder, Berlin and Vienna, 1912.

9. Wollstein and Bartlett: A Study of Tuberculous Lesions in Infants and Young Children, Based on Post-Mortem Examinations, AM. JOUR. DIS. CHILD., November, 1914, 362.

10. Addison and How: Am. Jour. of Anat., 1913, xv, 199.

11. Ridella: Ref., Ztschr. f. Kinderh., 1914 (Ref.), viii, 342.

12. The case of Strauss (Ztschr. f. Fleisch- u. Milch-Hygiene, 1910, xx, 129) quoted by V. Reuss (Die Krankheiten des Neugeborenen, Berlin, 1914, p. 452) proved on investigation not to be one of human tuberculosis.

than the one here reported (Sabouraud,¹³ Honl,¹⁴ Lehmann,¹⁵ Ustinow,¹⁶ Auché and Chambrelent,¹⁷ Stoeckel,¹⁸ Wollstein,¹⁹ Lobenstine,²⁰ Rollet,²¹ and Möller²²). Of these, only Wollstein's patient died of a disease other than the tuberculosis. In this instance the cause of death was bronchopneumonia and at necropsy scattered tubercles were to be found. This case suggests a close relation with the bacillosis previously mentioned. In all of this group the most advanced lesions were to be found in the periportal glands and the involvement of the abdominal organs was greater than that of the thoracic. In many instances the placenta was found to be involved. We have here unquestionably infection through the umbilical vessels.

In all the cases of both these groups tubercle bacilli were found either in the tissues or by animal experiment.

The clinical data are very scant. The cases of Stoeckel,¹⁸ Sabouraud,¹³ Lehmann,¹⁵ Honl,¹⁴ Ustinow,¹⁶ Auché and Chambrelent¹⁷ and Wollstein¹⁹ consist only in pathologic reports, the day of death being given in order, fourteenth, eleventh, first, fifteenth, uncertain, twenty-sixth and nineteenth. Of the other cases, two simply give besides the pathologic findings, the weight at birth and the day of death. In the case of Harbitz⁶ the child weighed 1,400 gm., was 47 cm. long, and died on the twenty-fifth day. In that of Rollett²¹ the child weighed 3,600 gm., was 51 cm. long, and died in forty-eight hours. The other three cases are somewhat more specific in their statements. That of Brindeau⁷ occurred in a baby whose birth weight was 2,150 gm. It was taken from the mother immediately. The child was cyanotic, somewhat edematous, and had a rectal temperature of 36 C. It remained cyanotic and died on the twelfth day. The spleen was normal in size, the liver somewhat enlarged and hard, and at necropsy was shown to weigh 190 gm. Miliary tuberculosis of the lung was found. The sections were very rich in bacilli. The second case is that of Lobenstine.²⁰ It occurred in a bottle-fed baby who died on the nineteenth day. At birth the child weighed 2,100 gm., at time of death, 1,650, showing a loss of 450 gm. The child was bottle-fed, showed a subnormal temperature throughout life, and had no cough nor diarrhea. An acute miliary tuberculosis was found at necropsy. The third case is that of Möller.²²

13. Sabouraud: *Compt. Rend. Soc. de Biol. de Paris*. 1891, xliii, 674.

14. Honl: Cited by Warthin and Cowie (Note 1).

15. Lehmann: *Berl. klin. Wehnschr.*, 1894, xxxi, 646.

16. Ustinow: *Arch. f. Kinderheilk*, 1898, xxv, 66.

17. Auché and Chambrelent: *München. med. Wehnschr.*, 1898, xlv, 616.

18. Stoeckel: *München. med. Wehnschr.*, 1904, li, 177 and 454.

19. Wollstein: *Congenital Tuberculosis*: *Arch. of Ped.*, 1905, xxii, 321.

20. Lobenstine: *Bull. Lying-In Hosp., City of N. Y.*, 1905, ii, 9.

21. Rollett: *Wien. klin. Wehnschr.*, 1913, xxvi, 1274.

22. Möller: *Arch. mens. d'Obst. et de Gyn.*, 1914, iii, 1.

The temperature was normal throughout. Respiration was short and labored, but there were no cyanotic attacks. The infant did not nurse well. The mother left the hospital with a tuberculosis of the uterus and died within two months of a general miliary tuberculosis.

From these meager data it is absolutely impossible to draw any definite conclusions as to the symptomatology of tuberculosis in the newborn. It is evident that Lobenstine's patient was a premature baby, or at least one congenitally debilitated, which would account very well for the subnormal temperature which existed throughout, since such an occurrence is not at all rare in infections of infants of this type. One would scarcely expect such a reaction in a baby of the size and vigor of the one we report. It is not at all impossible, too, that the early temperature in our case had nothing whatever to do with the tuberculosis, but was simply the so-called "inanition fever," which is so frequently encountered at this time. The enlargement of the liver, as mentioned by Brindeau, and present in our case, is a suggestive symptom, especially when combined with an irregular temperature existing from birth on. The combination of enlargement of the spleen, high, irregular temperature and enlargement of the liver, together with tuberculosis in the mother, is suggestive. In all cases except the one here reported and that of Möller the tuberculosis in the mother was as severe as that of the child, the date of death of the parent being only a few days before or after that of the child.

DIAGNOSIS

In the diagnosis of this affection very little can be expected from the ordinary tests. In the newborn the Pirquet test has proven negative almost without exception. Zarfl reports a positive *Stich-Reaction* in a baby, 17 days of age. Recently at the County Hospital one of us has been able to obtain a positive von Pirquet reaction in a premature infant, 16 days of age, whose mother was in the tuberculosis hospital. In another instance the reaction was positive on the nineteenth day. This, however, would give us little encouragement in the first few days of life, and hence the tuberculin reaction must probably be disregarded as a definite diagnostic means at this time. Since in many instances tubercle bacilli are found in the blood, a blood culture or the injection of blood into animals might be suggested. This offers three difficulties: first, that of obtaining blood from these young infants; second, the fact that the presence of the condition is rarely suspected, and, third, any animal thus experimented on succumbs to the tuberculosis only after the patient. It would seem, then, to be very difficult to arrive at a certain diagnosis in such cases, even though the case were suspected.

PROGNOSIS AND TREATMENT

As to the prognosis, tuberculosis of the newborn has been up to this time always fatal so far as we can tell. Sitzenfrey²³ reports four cases of tuberculosis of the placenta, however, in three of which the infants died at six weeks, three and six months, respectively; but the fourth remained alive during nine months' observation, and showed no symptoms of tuberculosis. It would seem, then, that the mere presence of tubercle bacilli in the placenta did not mean a tuberculosis of the fetus in all instances. The duration of life has varied from twenty-four hours to twenty-five days. It is very likely that children suffering with congenital tuberculosis may live as long as three to six months. The only clinical data on any case approaching this age is that given by Veszpremi.²⁴ The premature infant died on the thirty-seventh day, and from birth on had a temperature varying between 36.5 to 38.3 C. (from 97.7 F. to 101 F.).

Of course, treatment at present, in a condition of such extreme severity and of the nature of which tuberculosis of the newborn is, must necessarily be without results.

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23. Sitzenfrey: *Die Lehre von der kongenitalen Tuberkulose mit besonderer Berücksichtigung der Plazentartuberkulose*, Berlin, 1909.

24. Veszpremi: *Centralbl. f. allg. Path. u. path. Anat.*, 1904, xv, 483.

PROGRESS IN PEDIATRICS

LITERATURE OF 1913 AND 1914 OF INFECTIONS OF THE GENITO-URINARY TRACT IN CHILDREN

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VULVOVAGINITIS

Sources of Infection

Taussig,¹ in a report of sixty-six cases of vulvovaginitis treated in the Washington University Gynecological Dispensary, writes that "a correct appreciation of the etiological factors can only be obtained by considering the anatomy and histology of the lower genital tract in girls before puberty." The epithelium is not only much more delicate than in the adult, but is also far more open to infection, owing to the small size of the labia majora and the absence of hair. "In analyzing the possible causes of this infection we must consider first the source, and second, the manner of transmission." "The first question is whether the parents are the source of infection." In only two cases did the mother have a discharge, and further, only two patients were under 1 year of age, at which time they are most exposed to infection by the mother. He considers that "other already infected girls of the same age" are "the most important factor in the spread of the disease."

Under manner of transmission he considers rape, which is rare; the hand of an infected mother or other person, which is not common, and finally clothing, which is unlikely because of the inability of the gonococcus to withstand drying. "Being primarily concerned with home cases" he leaves out the common bath-tub as a means of spreading the disease, but does lay great stress on the danger of infection from the ordinary water closet seats which are built "so high that the smaller children in using them are forced to have their genitals and clothing rub over a considerable portion of the seat." The greatest danger is in the tenement houses and public schools. Taussig does not give "figures regarding etiology from the social service investigation of the cases, because the evidence on which they were based varied so much in reliability." However, "forty-seven out of sixty-six girls were of school age or over."

1. Taussig, F. J.: Am. Jour. Med. Sc., 1914, cxlviii, 480.

R. M. Smith² has studied the sources of infection through home visits by a social worker, and gives the following table based on thirty cases:

| | |
|-------------------------------------|---------------------------|
| Undetermined | 5 cases = 16.6 per cent. |
| Hospital infection | 1 case = 3.3 per cent. |
| Playmates | 4 cases = 13.3 per cent. |
| Assault | 4 cases = 13.3 per cent. |
| Other members of family infected... | 16 cases = 53.3 per cent. |

Over half the cases were apparently due to infection from other members of the family, in which Smith's findings disagree with Taussig's opinion, though the two agree that hospital and institutional cases are a minority. Smith says, however:

Bad habits are taught young children by those older than themselves, in some instances by those old enough to understand fully the significance of sexual matters. Masturbation is extremely common among the infected cases. Whether as a result of this or not . . . many of these children are sexually precocious. . . . I am confident that as we learn more intimately the history of infected children the less often we shall have to attribute the infection to toilets or other indefinite sources.

The same author also emphasizes the great influence of feeble-mindedness both in the children and in adults, finding that "in five of our [thirty] patients the infection is directly traceable to feeble-minded individuals, and two other patients were themselves feeble-minded."

Barnett³ has analyzed fifty cases from the Mount Sinai Hospital in New York, and gives the following figures:

| | |
|--|--------------|
| Discharged from hospital or other institution..... | 36 per cent. |
| Sleeping with mother who has a vaginal discharge.. | 18 per cent. |
| Sleeping with sister who has a vaginal discharge.. | 10 per cent. |
| Cases of unknown origin..... | 36 per cent. |

Spaulding,⁴ reporting eighty-three cases from the special clinic at the Children's Hospital in Boston, gives a somewhat similar list:

| | |
|-------------------------------------|--------------|
| Discharged from hospital..... | 21 per cent. |
| History of discharge in parent..... | 35 per cent. |
| History of contact | 4 per cent. |
| Not discovered | 40 per cent. |

Sinclair⁵ examined eighty-three babies at the Babies Hospital of Philadelphia and found that 19 per cent. were infected or highly suspicious on admission, and that 8.4 per cent. developed the disease in the hospital or the convalescent home.

On the whole, the recent trend, notwithstanding the great importance of hospital and institutional epidemics, would seem to place the

2. Smith, R. M.: Vulvovaginitis in Children, *AM. JOUR. DIS. CHILD.*, November, 1913, p. 355.

3. Barnett, N.: *Arch. Pediat.*, 1913, xxx, 650.

4. Spaulding, Edith Rogers: Vulvovaginitis in Children, *AM. JOUR. DIS. CHILD.*, March, 1913, p. 248.

5. Sinclair, J. F.: *Arch. Pediat.*, 1914, xxxi, 29.

ultimate responsibility further back, in the home, the school and the street or playground.

We must recognize that we are dealing not only with a medical disease but also with a social evil, and that the medical treatment alone is only a part of what needs to be done. This means that we must establish a close cooperation with the social workers in their attempt to solve the delicate questions of venereal disease.²

Prophylaxis

The medical profession is just beginning to realize the great number of endemic cases in the cities and the difficult nature of the problem. The health commissioner of New York, Dr. Goldwater, has recently made a preliminary report on the question, of which the following is an extract.⁶

That a form of vaginitis which is bacteriologically indistinguishable from gonorrheal vaginitis is a common condition among children in this city and elsewhere, is well known to clinicians.

If a serious attempt were made to exclude from school all children who suffer from vaginitis, it would be necessary (a) to establish the machinery by which a complete physical examination of all female school children could be made; (b) to convince the public of the necessity of the proposed measure; (c) to establish the legal and moral right of the city authorities to require such an examination. Furthermore, inasmuch as the condition in question is one which, notwithstanding the most intensive treatment, often persists for months and even for years, it would be necessary to inaugurate a method by which the education of excluded children could be continued. The only logical method would be to send private teachers into the houses of infected children.

The questions here involved are among the most difficult and puzzling with which public health administrators have to deal. I am not aware that the problem has been solved anywhere, and can only promise, on behalf of this department, unremitting attention to it, in the hope that a working program may ultimately be formulated.

Taussig¹ writes that "Gonorrhea in little girls . . . is simply the result of inadequate sanitary precautions," and offers the following suggestions "as additional preventive measures for the control of this disease":

1. The instillation of a drop of 2 per cent. silver nitrate solution in the vestibulum vaginae of all new born girls whose mothers show evidence of gonorrhea.

2. Making vaginitis in children a disease reportable to the Board of Health. . . . We would not be justified in excluding the children from school for eight or nine months . . . , unless there existed a special school . . . where [they] could be given . . . instruction.

3. Instruction of parents of infected children through the visiting nurse regarding preventive measures to limit the infection.

4. Investigation by the visiting nurse as to the probable origin of the infection in each case with a view to excluding this factor from contaminating other children in the same house.

5. The adoption of a U-shaped seat with low bowl and other precautionary measures to prevent the spread of infection through the public lavatories in schools, playgrounds, comfort stations and tenements. I consider this last named suggestion the most important of all. . . .

6. Goldwater, S. S.: *Modern Hospital*, 1914, ii, 305.

Taussig also as well as Barnett³ advises the use of paper coverings for lavatory seats.

These are the most radical recommendations yet made. Most authors^{4, 2} content themselves with keeping the children out of school for a week or two, and warning the teachers and school nurses when they go back that they are not to use the toilet. G. G. Smith⁷ adds that with "this danger removed [i. e., the common toilet] they are less likely to be a focus of infection while in school than when playing untended on the street."

Diagnosis

Sinclair⁵ examined eighty-three girls under 3 years of age consecutively admitted to the Babies Hospital of Philadelphia, and reports that scraping the vagina with a platinum loop was the most efficient method of obtaining a positive smear. Rinsing of the vaginal vault with a 1:5,000 mercuric chlorid solution and examination of the centrifugalized sediment of the collected fluid was not satisfactory. Of the positive or suspicious cases 21.7 per cent. would have escaped detection without examination with the urethroscope.

Barnett³ uses a speculum and mirror to aid him in getting scrapings of the vagina with a platinum loop.

Treatment

The general opinion seems to be that children with vaginitis do better if they are kept in bed or very quiet during the first few weeks and then if particular attention is paid to improving their general condition. Further than this there is the greatest possible disagreement as to treatment. Kerley,⁸ as an example of one type of procedure, uses nothing but a cleansing douche of warm boric solution four times a day followed by a thorough drying and dusting with boric acid starch and zinc. He believes "that gonorrheal vaginitis is a self-limited disease, and that something takes place during the child's life that makes the vagina less hospitable to the gonococcus." Hamilton⁹ also, as far as the local treatment goes, does nothing but "keep the patient clean and dry."

Barnett³ uses a daily permanganate douche given at home by the mother or a visiting nurse, and follows it three times a week by an endoscopic treatment of the cervix and vagina with Lugel's solution. He also gives hexamethylenamin. He concludes that

7. Smith, George Gilbert: The Treatment of Gonococcus Vulvovaginitis, with Further Observations on the Value of the Complement Fixation Test in the Management of this Disease, *AM. JOUR. DIS. CHILD.*, March, 1914, p. 230.

8. Kerley, C. G.: *Arch. Pediat.*, 1913, xxx, 702.

9. Hamilton, A.: *Arch. Pediat.*, 1913, xxx, 702.

The first important fact to bear in mind in treating this disease is the infection of the cervix and the difficulty of reaching this nidus of infection by the ordinary methods of treatment. Any infection of the cervix is difficult to treat because of its inaccessibility to the child. The simplest method . . . , irrigation of the vagina, is neither practical nor of great value. The affected parts are not reached directly, and the treatment must be continued for too long a time Direct applications must be made to the deep point of infection. Cures can be obtained by the treatment of the cervix . . . in a short period of time, and strong solutions can be applied to the cervix and vaginal walls directly without causing any pain.

Spaulding,⁴ G. G. Smith,⁷ and R. M. Smith² all favor a daily cleansing douche followed by the instillation of some silver preparation. G. G. Smith⁷ adds that after the injection the child should lie on her back for at least fifteen minutes with her hips elevated and thighs pressed together. He also, in persistent cases, makes direct applications to the cervix through an endoscope, using either tincture of iodine or a silver solution. Taussig¹ omits the douche, but uses locally 25 per cent. argyrol or a solution of silver nitrate, from 2 to 4 per cent.

Rubin and Leopold¹⁰ are the strongest exponents of the necessity of endoscopic treatment. They have made a careful study of fifty cases "under extended observation and under various treatments, including . . . all known therapeutic remedies." They made use in every case of the electric lighted female urethroscope and "have shown that the infection involves the vagina and the vaginal portion of the cervix." They suggest that:

1. It is important to determine the extent of the deep lesion before any active treatment is begun. For this purpose the electric lighted female urethroscope should be used.

2. By means of the same instrument appropriate medication can be carried out.

3. When irrigations are resorted to the douche tip or catheter should enter the vagina at least 1½ inches.

4. Applications by means of swabs used alone are useless and injurious.

5. When strong silver solutions are applied to the cervix and vagina it is well to keep the patient in bed for a few days.

Mattisohn,¹¹ however, considers that "cervix involvement is not proven."

There is also considerable disagreement about the use of vaccines. Hamilton⁹ says she is "still enthusiastic in the treatment of recent cases by vaccines." Comby and Condat¹² give the case reports of sixteen girls with gonorrheal vulvovaginitis and one boy with urethritis, all treated with Nicolle's vaccine, which is a mixture of one part gonococci to nine parts of a similar symbiotic Gram-positive coccus. "The hos-

10. Rubin, I. C., and Leopold, J. S.: On the Cause of the Persistence of Gonorrheal Vulvovaginitis in Children, *AM. JOUR. DIS. CHILD.*, January, 1913, p. 58.

11. Mattisohn: *Arch. f. Dermat. u. Syph.*, 1913, cxvi, 817.

12. Comby, J., and Condat: *Arch. de méd. d. inf.*, 1914, xvii, 419.

pital patients remained in bed," but "all local treatment was omitted." "Improvement is in general rapid. After the second injection, sometimes after the first, the diminution in the discharge is very clear; progress thereafter is slower and less regular, and seven injections at least are necessary to obtain a satisfactory result." In recent cases the authors obtained an apparent cure, "but the results in older girls were uncertain." "This method . . . allows the omission of douches, so badly tolerated . . . and so often impossible to entrust to the mother." "In certain more tenacious forms the two treatments can . . . be combined; but, in recent cases, vaccine therapy would seem sufficient."

Spaulding⁴ has tried out vaccines in thirty-five cases, in addition to the local treatment. Autogenous preparations she found no better than stock. She concludes that "in our hands vaccine has not proved a specific . . . However, we do feel that it is an additional factor for good . . ."

Barnett,³ on the other hand, treated fourteen of his fifty cases "with vaccines at intervals of three to seven days in doses of from 5 to 100 millions," and reports that "none of my cases treated with vaccines showed any improvement as to the vaginal discharge."

Heyman and Moos¹³ have reached a similar opinion, saying "in open lesions of urethral and uterine mucous membranes it has failed entirely."

Hamburger¹⁴ reports on twenty-one cases in all of which the patients were kept in bed without local treatment during the administration of vaccines. "Five children were given three to four intravenous injections. To this method . . . we must take exception because of the severe . . . reaction. All other injections were intramuscular . . ." He concludes that "The treatment of vulvovaginitis by vaccines alone is absolutely and entirely insufficient to replace local treatment."

Reinfection or Relapse

Spaulding⁴ is frankly pessimistic in her belief as to the great frequency of relapse. Of twenty-six cases "all but two had a recurrence of the discharge after intervals varying from three weeks to six months, and one of these two had a vulvovaginal abscess after the discharge had ceased, strongly suggesting that the infection was still present." "We believe . . . that the disease may extend over many years, during which time there may be many recurrences, and that the periods

13. Heyman, H., and Moos: *Monatschr. f. Geburtsh.*, 1913, xxxvii, 632.

14. Hamburger, R.: *Deutsch. med. Wchnschr.*, 1914, xl, 759.

of latency may be as long as eighteen months," and "that the most efficient treatment does not insure a permanent cure."

Mattisohn¹¹ says that "the prognosis [is] . . . rather favorable for a final cure, [but that] proper treatment takes at least four to six months, often much longer, a permanent cure can be spoken of only if after months or years no gonococci are recognizable."

Barnett's³ definition of cure is three negative vaginal smears one week apart.

G. G. Smith,¹⁵ in his first paper, writes:

A study of twenty-five cases of vulvovaginitis by means of the complement fixation test shows that the test was positive in eleven out of twelve clinically positive cases, and in four cases in which the evidence was inconclusive. It was negative in three cases in which other evidence of cure was insufficient, but in seven others the clinical findings were corroborative. We are of the opinion that for the purpose of establishing a cure, the test is of considerable value.

A year later, the same author⁷ strongly opposes Spaulding's views of the frequency of relapses, arguing that in her cases "the test of cure was insufficient." He writes that "if after three or more months, during which frequent smears from the depths of the vagina have contained no pus, and all other signs of the infection have disappeared, a discharge containing gonococci recurs, we believe that this attack is frequently a reinfection, very possibly from the same source as the first."

R. M. Smith² says that "when the original source of infection still exists and no reform has taken place in the habits of the patient, a reinfection may easily occur and seems . . . more likely than that a relapse has taken place."

GONOCOCCUS INFECTION IN BOYS

Smith and McKee¹⁶ report a case of urethritis in a boy of 17 months. Gonococci were found in smears and in culture. The source of infection was probably the nurse.

Nicoll and Wilson¹⁷ describe a case of arthritis in a boy of 2½ years, following scarlet fever. Two of the joints became purulent and had to be opened. To their great surprise gonococci were found in the culture. Blood cultures were negative. The urethra appeared normal in every way, but two out of five cultures taken from it contained gonococci.

15. Smith, George G.: The Complement Fixation Test in the Management of Gonococcus Vulvovaginitis, *AM. JOUR. DIS. CHILD.*, April, 1913, p. 313.

16. Smith, A., and McKee, C. S.: *Brit. Med. Jour.*, 1913, i, 878.

17. Nicoll, M., Jr., and Wilson, M. A.: *Jour. Infect. Dis.*, 1913, xii, 52.

PYELITIS

Mode of Infection

Thomson¹⁸ in an excellent paper based on seventy-one cases of colon infection of the urinary tract in his private practice, says:

It is scarcely ever possible to decide in any individual case which route the bacilli takes in passing from their original harmless position to where they ultimately set up disease. It is, however, quite certain that they are sometimes carried there by the blood stream, sometimes pass in by the lymphatic channels, and sometimes ascend from outside by the lumen of the urinary tract.

When the bacilli reach the urinary tract . . . they are either washed out immediately . . . , or else destroyed . . . ; or they may remain for a time doing little or no harm. . . . If the virulence of the organisms has been increased by morbid processes in the intestine, or otherwise, or the normal resistance of the tissues lowered by local or general disease; or perhaps if there has been some retardation of the flow of urine . . . , then more or less violent inflammation . . . may be set up.

He then analyzes the sex incidence of the disease, making the following points:

1. . . . the number of girls is much larger than that of boys; among my cases the girls formed 79 per cent.

2. In the young infants . . . the disease begins more often with diarrhea than in older children. . . . Diarrhea is more frequently a marked symptom in boys than girls. [That is] cases setting in during apparent good health are commoner in girls than in boys.

3. Further . . . during the first six months of life far more boys than girls are affected, although after the sixth month girls largely predominated. When we . . . analyze the ages and sexes of 224 babies under 2 years taken at random from thirteen authors we find that . . . there is still a considerably greater proportion of boys during the first six months than at any later age.

4. The extreme rarity of rigors at the onset . . . in boys is noteworthy . . . when compared with the frequency of this symptom in girls . . .

5. Mild cases of *Bacillus coli* infection are rare in boys in my experience. In male patients the attacks of pyelitis are apt to be severe, and there is usually in them a much larger proportion of cases of fatal pyelonephritis than among girls.

In discussing these five points, he writes:

. . . the great preponderance of female patients seems . . . to force us to the conclusion that ascending infection by way of the urethra must be a common occurrence; and the excess of girls over boys probably represents the frequency with which urethral infection takes place. It seems very unlikely that the colon bacilli can force their way up the lumen of the male urethra. The greater prevalence of antecedent diarrhea in boys would probably cease to exist if we were able to subtract from the list of girls the primary cases infected *per urethram*.

The frequency of pyelonephritis in the male sex may be explained by the infection having usually in them passed straight from the bowel to the kidney and pelvis, and not having ascended from below. The facts that rigors are so very rare in acute pyelitis in boys, and in pyelonephritis in both sexes, while they are so common in acute pyelitis in girls (in whom we suspect an ascending infection) suggest the idea that the ureters may be the particular portion of

18. Thomson, J.: Lancet, London, 1913, ii, 467.

the urinary tract from irritation of which a rigor most readily arises. The frequency with which rigors are met with in ureteral calculus may be held to support this view.

Somewhat similar views are held by Wyman,¹⁹ who, from a study of sixty-five cases at the Children's Hospital in Boston, concludes that the ascending route is the common one in girls, and the hematogenous in boys, while what he calls the transparietal is rare in both sexes. An analysis of the age and sex of his patients gives the following:

| | |
|----------------------------|----------------|
| Males under 2 years..... | = 37 per cent. |
| Females under 2 years..... | = 63 per cent. |
| Males over 2 years..... | = 10 per cent. |
| Females over 2 years..... | = 90 per cent. |

The views of F. H. Smith²⁰ are less clear; he writes that "in the younger children and babies the infection is apt to be the colon bacillus, and most often from direct fecal contamination of the vulva, or possibly, by more direct route through blood or lymph paths to the kidney, upset bowels preceding the illness being highly suggestive of increased toxicity of the intestinal flora." In older children, however, he considers that "repeated attacks of acute tonsillitis, acute bronchitis and 'kidney trouble,' in sequence, suggest their interdependence."

Freeman²¹ believes in the ascending road of infection, because of the predominance of female cases.

Green,²² however, writes that pyelitis "probably proceeds by lymphatic extension from the intestine," while "acute inflammatory nephritis . . . is most usually hematogenous in origin." Nevertheless he includes as predisposing causes "calculi, constipation, phimosis, anal fissures and foci of infection elsewhere."

Cannata and Caronia²³ emphasize the necessity of preventing the early infections. Habitual constipation is dangerous because there is usually elimination of bacteria by way of the urinary apparatus. Fecal contamination of the vulva, phimosis and foreign bodies in the bladder, are the sources of ascending infections. Chilling, or any trauma to the bladder, is likely to prove an exciting cause. Stiner²⁴ also mentions the dangers of chilling.

Langstein²⁵ has reported two cases of pyelitis complicating Hirschsprung's disease, and also as a sequel to pertussis a fatal pyelitis due to Friedlander's bacillus. He writes that "in the future the hematogenous

19. Wyman, E. T.: Boston Med. and Surg. Jour., 1914, clxx, 540.

20. Smith, F. H.: Old Dominion Jour. Med. and Surg., 1914, xix, 77.

21. Freeman, Rowland Godfrey: Urinary Analysis in the Diagnosis and Treatment of Diseases of Infancy and Childhood, Jour. Am. Med. Assn., Nov. 21, 1914, p. 1802.

22. Green, R. M.: Boston Med. and Surg. Jour., 1913, clxviii, 645.

23. Cannata, S., and Caronia, G.: *Pediatrics*, 1914, xxii, No. 9.

24. Stiner, O.: *Cor.-Bl. f. schweiz. Aerzte*, 1914, xlii, Nos. 23-26.

25. Langstein, L.: *Med. Klin.*, 1913, ix, 1491.

and lymphatic mode of infection will be placed more in the foreground."

Kowitz²⁶ is practically alone in believing that the ascending route of infection is uncommon as compared with the hematogenous or lymphatic. He was led to this opinion first by finding that his own cases did not show the customary predominance of girls; in forty cases he had seventeen males to twenty-three females. "This does not seem to be such an overwhelming predominance of females that we can speak of an essential difference between the sexes." He then discovered in his cases the marked relation to the time of year shown in the accompanying chart.

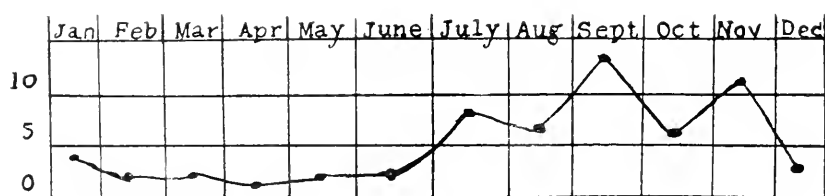


Chart showing relation of occurrence of pyelocystitis to time of year.

To prove pyelocystitis a descending hematogenous disease, it is necessary to find a source of infection elsewhere in the body; that is, the acute digestive upsets of the summer. Pyelitis does not accompany, but follows the diarrheas. The frequency of colon bacillus infection is to his mind another proof of the hematogenous mode of infection.

Clinical Symptoms

Wyman¹⁹ has analyzed carefully the symptoms occurring in his sixty-five cases and gives the following list:

| | |
|----------------------|-----------------|
| Vomiting | in 39 per cent. |
| Dysuria | in 36 per cent. |
| Pollakiuria | in 40 per cent. |
| Chills | in 15 per cent. |
| Abdominal pain | in 16 per cent. |

Furthermore, he has found that pyelitis occurred as a complication of other disease as follows:

| | | | |
|--------------------|---------|-------------------------------|---------|
| Otitis media | 8 times | Pneumonia | 7 times |
| Bronchitis | 2 times | Infectious diarrhea | 4 times |
| Typhoid | 2 times | Intestinal indigestion | 2 times |
| Measles | 2 times | Tuberculous peritonitis | 1 time |

Gordon²⁷ separates the cases according to their clinical signs into these five groups.

26. Kowitz, H. L.: München. med. Wehnschr., June 16, 1914, p. 1341.

27. Gordon, R. G.: Brit. Jour Child Dis., 1914, xi, 252.

1. Symptoms of general feverish disorders, without any indication that one special symptom was affected.
2. Cerebral symptoms.
3. Pulmonary symptoms.
4. Abdominal symptoms.
5. Urinary symptoms.

Langstein²⁵ has a similar classification based on the dominating clinical symptom; that is, a toxic type, a meningeal, a pulmonary, a gastro-intestinal type, one associated with icterus, and one which gives most of the signs of appendicitis. He also mentions a form of pyelitis in which the urine contains many red blood corpuscles and only a few pus cells and says that this "is frequently the cause of erroneous diagnosis."

Thomson¹⁸ and Marsh²⁸ both emphasize the frequency of chills or rigors, the former saying that he does "not remember ever having seen an infant under 2 years who had had a well-marked rigor and who had no pus in the urine"; and the latter, that "shivering . . . is exceedingly rarely met with in infancy, except in this condition."

Stiner²⁴ mentions redness and swelling of the external genitals together with inability to urinate, as the initial symptoms of pyelitis which is brought on by exposure to cold.

Urinary Findings

Langstein's²⁵ hemorrhagic type must be again mentioned, the sediment consisting of "many red blood corpuscles, only scattered leukocytes, and perhaps here and there a cast. At the time it is difficult to decide whether this is the picture of a hemorrhagic nephritis, a calculus or a beginning pyelitis. . . . There are cases which proceed directly to recovery, provided proper medical treatment is instituted at once."

Freeman²¹ endeavors to draw a line between a normal and a pathological number of pus cells in the urine. According to him "1-2 leukocytes in a D-field (Zeiss) of precipitate [of centrifugalized urine] from a female baby does not indicate a pyelitis That number in a male baby, or more in a female baby, should render the diagnosis suspicious." F. H. Smith²⁰ has a somewhat similar standard, although he does not find a difference between the sexes. He writes that "it is by no means exceptional to find as few [pus cells] as 3 to the $\frac{1}{6}$ field, and yet the symptoms be most severe."

Kowitz²⁶ has isolated the infecting organism in forty-four cases and confirms the predominance of the colon group, thus:

28. Marsh, N. P.: Brit. Jour. Child. Dis., 1913, x, 385.

| | |
|---|----|
| <i>B. coli</i> | 24 |
| <i>B. paracoli</i> | 10 |
| <i>B. lactis aerogenes</i> | 7 |
| Staphylococcus (cases of eczema and furunculosis) | 3 |
| Mixed | 3 |

Other authors have nothing new to add to the already well-known urinary picture.

Duration of the Disease

Thomson,¹⁸ Freeman,^{21, 29} Marsh,²⁸ Wilson³⁰ and others, agree that the disease may last untreated for several years and show few or no symptoms. It may flare up at any time, however. With correct treatment, Langstein²⁵ considers that 90 per cent. of the patients recover. In severe cases the patients may recover completely after three and one-half years, or the condition may lead to a contracted kidney or to a nephrosis. Marsh²⁸ gives a favorable prognosis, but adds that "before pronouncing the patient cured, the urine should not only show an absence of organisms and of pus cells, but should also be culturally free . . ." "In spite of all treatment, many cases become chronic; in these acute exacerbations alternate with long periods of quiescence, but the urine never becomes entirely free from pus cells and organisms."

Treatment

The one form of treatment against which no dissenting voice is raised is the administration of large quantities of fluid. Further than this, there is apparently no specific treatment. In many of the acute cases the patients get well untreated.

Thomson¹⁸ gives sufficient potassium citrate to maintain an alkaline reaction in the urine. Marsh²⁸ and Wyman¹⁹ agree with this procedure. The latter, however, favors changing the reaction of the urine back and forth by the alternate administration of potassium citrate and sodium benzoate. Freeman²⁹ says that "the alkaline treatment of pyelitis, while it is safe and will control many cases, is markedly less efficient than other methods of treatment. Langstein²⁵ goes so far as to say that alkalis are useless in the treatment of the disease.

Probably the best of the so-called "urinary antiseptics" is hexamethylenamin. It is pretty generally agreed now that it acts only in an acid medium. Freeman^{21, 29} considers it an "absolute antiseptic for certain infections of the urinary tract." He begins always with small doses of from $\frac{1}{2}$ grain to 2 grains several times a day, and then increases rapidly, being careful to watch the child and its urine for symptoms of irritation of the kidneys. "Large doses of hexamethyl-

29. Freeman, Rowland G.: The Diagnosis and Treatment of Pyelitis in Infancy, AM. JOUR. DIS. CHILD., August, 1913, p. 117.

30. Wilson, H. W.: Brit. Jour. Child. Dis., 1913, x, 289.

enamin should not usually be continued for more than a week at a time, and then after several days without any treatment, or with alkaline treatment, it should be started at the maximum dose given before and the amount increased daily until an influence on the urine is obtained. Doses of 25 grains daily in a child of 6 months, and 35 to 45 grains a day in a child of 9 to 12 months, may be safely given in this way to some infants." Wyman,¹⁹ as second choice to the alkaline treatment, gives hexamethylenamin and sodium benzoate. Cannata²³ uses hexamethylenamin alone or alternating with phenyl salicylate (salol), offering at the same time large amounts of an acid drink such as diluted hydrochloric or phosphoric acid. Marsh²⁸ and Thomson,¹³ representing the English point of view, are sceptical about the value of hexamethylenamin and phenyl salicylate. Kowitz²⁶ considers all urinary antiseptics useless, while Langstein²⁵ admits that hexamethylenamin may be of value as a prophylactic, but that "in severe cases more is accomplished by salol, in not too small doses (0.6 gm. to 1.0 gm. per diem)."

The value of vaccine therapy is still much disputed. Freeman,²⁹ writing in 1913 of renal infections with the colon bacillus, says: "Vaccines, either autogenous or commercial, are useful in controlling the constitutional symptoms of pyelitis." After another year's experience, he adds²¹ that they "produce a reduction in the temperature; but, so far as I know, the vaccines do not cure the disease, although they apparently cure it. The child loses its fever and will increase in weight and seem perfectly well, but when the urine is examined one finds the same pus and bacteria as before." Green²² and Wyman¹⁹ also advise vaccines, but only in resistant cases. Marsh²⁸ and Kowitz²⁶ are doubtful about their value. Wilson³⁰ reports a case in which autogenous vaccines were used without success. The parenchyma of the right kidney finally became involved, abscesses formed, and a nephrectomy was done which was followed by prompt recovery. Thomson¹³ reports that he has "used vaccines in a few cases, but with disappointing results." Langstein²⁵ has not only never seen good results from vaccines, but has also "seen a child on the second injection suddenly become very sick, with a high temperature and bloody stools." He considers that this may have been very probably an anaphylactic phenomenon.

TUBERCULOSIS

Renal tuberculosis in children is a very rare disease. Oraison³¹ reports three new cases, all in girls, bringing the total number of reported cases up to fifty-one. One of his patients had a severe Pott's

31. Oraison, J.: *Jour. d' urol.*, 1913, iv, 15.

disease, was not operated on, and died; the other two had nephrectomies; one apparently recovered and the other was lost sight of. Rocher and Ferron³² report a case, also in a girl, in which the offending kidney was removed with resultant cure. For diagnosis both articles advise cystoscopy and ureteral catheterization. It is surprising at what an early age this is possible, that is, in girls after 5 years,³² and in both sexes after 6 or 7 years.³¹ "The urethra admits easily a No. 40 tube 7 cm. long, and, in spite of the reduced field, the shortness of the tube permits the exploration of the bladder . . ." "The ureteral opening admits usually a No. 6 or No. 7 sound." "We have frequently employed general anesthesia, not because these manœuvres are painful, but because the children became very often unmanageable with fright at the sight of the instruments."³² "Finally, the treatment of renal tuberculosis in childhood presents nothing unusual . . . It is better, even for an infant, to live with a single healthy kidney than with both kidneys, one of which is diseased and the other constantly threatened."³¹

Primary genital tuberculosis is also rare. Oliver Lyons³³ reports three cases in small boys. In two of these the infection was in epididymis and the patients appeared to be in perfect health. The onset was sudden with pain on palpation, edema of scrotum, effusion into the tunica vaginalis and enlargement of the testicle. "In the case in which the prostate and seminal vesicles were found infected, frequent urination was the first symptom noticed by the mother, but as the case progressed the irritability became so marked that the patient was unable to retain his urine more than twenty or thirty minutes at a time." Also, in contrast to the other two, he "presented a typical tuberculous appearance." From a study of his cases and of the literature, Lyons concludes:

For the true conception of these cases it is important to know that tuberculosis of these organs remains almost always the only tuberculous focus in the body; differing from later periods of life when it is frequently secondary to other processes in the genito-urinary tract. Therefore operation may produce permanent cure, although this is not always certain.

Graefe³⁴ has analyzed the necropsy protocols of eighty cases in all ages which showed tuberculous lesions in the female genitalia. He found nineteen of these to be in girls under 15 years old, which is a surprisingly high number. He studied these nineteen cases further and found that in all the lesions in the genitalia were secondary to tuberculosis elsewhere in the body. The distribution of the lesions was as follows:

32. Rocher, H. L., and Ferron, J.: *Jour. d' urol.*, 1913, iii, 153.

33. Lyons, Oliver: Tuberculosis of the Genital Organs in Children, *Jour. Am. Med. Assn.*, Dec. 6, 1913, p. 2051.

34. Graefe, G.: *Monatschr. f. Geburtsh.*, 1914, xl, 448.

| | No. Cases | Per Cent. |
|--|-----------|-----------|
| Uterus only | 0 | = 0 |
| Cervix | 0 | = 0 |
| Tubes only | 5 | = 26.3 |
| One tube only | 3 | = 19.2 |
| Both tubes only | 2 | = 10.5 |
| Uterus and both tubes..... | 14 | = 73.7 |
| Both ovaries | 3 | = 19.2 |
| One ovary alone | 0 | = 0 |
| Uterus, both ovaries and both tubes..... | 3 | = 19.2 |
| Vagina | 1 | = 5.3 |
| Vulva and clitoris | 0 | = 0 |

"This table shows that in girls as in women the tubes are the most frequent site of genital tuberculosis."

The same cases classified according to age, give this result:

| | |
|--------------------|---------|
| Under 1 year | 1 case |
| 1- 5 years | 9 cases |
| 5-10 years | 2 cases |
| 10-15 years | 7 cases |

The author has no explanation of the high figure for the 1 to 5 year period. The increase after 10 years, however, is probably due to the influence of puberty.

Holt³⁵ has reported a case of miliary tuberculosis following a ritual circumcision:

A healthy child, born of healthy parents, breast fed, developed local symptoms of infection within a few days after the operation and these persisted, being followed after a few weeks by symptoms of general infection which continued until death. The lesions found at the necropsy point strongly to a spreading of the infection through the lymphatic system beginning from the wound, and afterward to a general blood infection.

He abstracts the 40 previously reported cases, and says that of the 41 patients, 16 are known to have died, 7 are tuberculous, in 12 the final results are not known, and only 6 are stated to have recovered. For the treatment, he advises the early removal of the inguinal glands. He concludes "that syphilis is less frequently acquired in this manner than is tuberculosis," and that "it is the duty of the physician to raise his protest against the performance of ritualistic circumcision in every case."

Champtaloup³⁶ reports from New Zealand a similar case, except that the operator was a physician who has since died of laryngeal tuberculosis. The child was 7 weeks old at the time of the operation. The wound suppurated badly and after three weeks an abscess formed in the right groin. Another small abscess appeared in the skin and the child became emaciated and hectic. Champtaloup first saw the child when it was 10 months old, at which time smears and cultures of the pus were negative, although guinea-pigs inoculated at the same time

35. Holt, L. Emmett: Tuberculosis Acquired Through Ritual Circumcision. Jour. Am. Med. Assn., July 12, 1913, p. 99.

36. Champtaloup, S. T.: Brit. Med. Jour., 1914, i, 814.

showed a well marked tuberculosis in four weeks. The patient was treated with tuberculin and when seen eight months later was the picture of health.

PSEUDOTUBERCULOSIS

Scherber³⁷ has described an acute inflammation of the vulva which leads to an ulceration resembling tuberculosis. It heals readily under cleanliness and mild antiseptics.

RHEUMATIC ORCHITIS

Bass³⁸ describes a boy $2\frac{1}{2}$ years old who developed erythema nodosum and torticollis and four days later, while under salicylates, the scrotum suddenly swelled. "Examination showed the scrotum . . . twice its normal size. Marked local heat. Skin of scrotum edematous and dusky in color." The left testicle was enlarged and exquisitely tender, the right normal. The condition quickly disappeared and a month later there was "no atrophy of the testis."

329 Beacon Street.

37. Scherber, G.: *Wien. klin. Wchnschr.*, 1913, xxvi, 1070.

38. Bass, M. F.: *Acute Rheumatic Orchitis . . . Associated with Erythema Nodosum and Acute Torticollis in a Child Aged Two and One-Half Years*, *Jour. Am. Med. Assn.*, May 21, 1913, p. 1608.

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THE MODE OF INFECTION AND ETIOLOGY OF EPIDEMIC POLIOMYELITIS*

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I

The two problems of uppermost interest in respect to epidemic poliomyelitis are: first, the mode of infection, and second, the nature of the specific microorganism causing the disease. I propose to deal briefly with these two aspects of the subject.

Two views are entertained regarding the mode of infection; according to one the infectious agent of the disease is communicated by personal contact; according to the other, it is conveyed by the stable fly. The differences involved in these two conceptions are fundamental, and hence the practices looking toward prevention of the malady based on them must be wholly different, if they are to achieve the result desired. For that reason it is imperative that the validity of the two doctrines be carefully scrutinized and appraised.

Let us examine first the evidence available bearing on the insect conveyance of the disease. This notion was suggested, in the first place, by the seasonal prevalence of epidemic poliomyelitis, which is predominantly a disease of midsummer and early autumn. However, it is not strictly speaking thus narrowly limited in incidence, since cases occur in the spring and even in the winter months, although they are few in number.

In the second place, the notion is supported by the rural character of some epidemics, as well as by the relatively wide distances which separate many of the cases. In these instances, however, the peculiarities are of degree rather than kind. Epidemics of poliomyelitis prevail also in towns and cities, and cases may be closely associated as well as widely separated.

The notion of insect carriage received for a time the support of experimental evidence, without which it would have remained merely a suggestive possibility; and the wide currency which this notion has

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obtained among the laity depends wholly on an imperfect experimental foundation which has now been largely disproved.

At the Congress of Hygiene and Demography held in Washington in 1912, Dr. M. J. Rosenau of the Harvard Medical School announced, as will be recalled, that he had succeeded in communicating experimental poliomyelitis to several monkeys by permitting stable flies to feed first on monkeys inoculated intracerebrally with the poliomyelitic virus, and then on normal monkeys. Although the studies which he reported were then incomplete and he made his announcement in a judiciously tentative fashion, he expressed the opinion that the flies might carry the infective agent, and also that in conveying it from one human being to another an intervening period of time was necessary, during which the virus underwent some change of development within the insect host. This announcement was followed very quickly by a confirmatory one emanating from Anderson and Frost of the U. S. Public Health laboratory in Washington.

No satisfactory explanation of the successful experiments performed by Rosenau and by Anderson and Frost has thus far been offered, since in no other instance have confirmatory results been obtained. The great importance of the subject led immediately to a repetition of the experiments in several laboratories in this country and in certain laboratories abroad, without yielding a single instance of positive infection. Moreover, Anderson and Frost themselves a little later announced that they had failed subsequently to repeat their earlier successful experiments.

Without pursuing this topic further, we may now turn our attention to the other conception, namely, that infection in poliomyelitis is conveyed through personal contact. In considering that view of the mode of infection it is necessary at the outset to have an understanding of the clinical types of poliomyelitis. So long as the affection was conceived of as a frankly paralytic disease in all instances, it was impossible to trace the connection of cases one with another, but once it was determined—as was done by Wickman—that epidemic poliomyelitis assumes non-paralytic and ambulant forms, the subject of the mode of infection was opened up to restudy and to a wholly new interpretation.

The proof of the existence of abortive and ambulant forms of poliomyelitis is not clinical merely, but depends also on laboratory findings. The several laboratory findings may be stated briefly to be the following: the detection of changes in the cerebrospinal fluid; the demonstration of neutralizing immunity principles in the blood; and the determination of the presence of the virus of poliomyelitis on the upper respiratory mucous membrane. The changes in the cerebrospinal

fluid consist of increased cellular content and the presence of globulin; the two conditions may coexist. The new cells are chiefly lymphocytes. The neutralizing properties of the blood depend on the appearance in the serum of immunity principles absent from the normal blood, which correspond to similar immunity principles arising after a frank attack of paralytic poliomyelitis. The virus of the disease has been detected on the nasal and pharyngeal mucous membranes in such quantity and quality as to make possible the communication of poliomyelitis to monkeys. The unmistakable demonstration, both by clinical observation and laboratory tests, of the existence of abortive and ambulant cases of epidemic poliomyelitis—many of which may and do escape detection—indicates how wide, indiscriminate, and unsuspected the distribution of the virus by personal contact may readily become.

But the facts now in hand carry us beyond the distributing power exercised by the frank and abortive ambulant cases, since it can now be affirmed that epidemic poliomyelitis is one of the diseases in which both healthy and chronic carriers of the microbic agent of infection arise. The few healthy carriers thus far detected consist of persons who have been in very close and intimate contact with persons acutely ill with poliomyelitis; for example, the parents of a paralyzed child. The few instances of chronic carriers now known consist of persons who have recovered from an acute attack, but in whom at the expiration of several months the virus has been detected, by animal inoculation, on the upper respiratory mucous membrane. The two classes last mentioned of potential carriers of the infectious agent add materially to the possibility of wide dissemination of the virus.

It is very important, now that the existence of healthy and chronic carriers of the infectious agent of epidemic poliomyelitis is established, that there should not arise undue concern regarding the dangers of conveying the disease, while the fact should be taken into account in devising measures for the prevention of the conveyance. Possessing as we do at present only the imperfect means of animal inoculation for detecting the virus of poliomyelitis, still it appears that the healthy and chronic carriers are not more numerous in this disease than in many other infections of more common occurrence.

Given, therefore, the possibility of the distribution of the virus being effected by, first, the frankly ill, second, the slightly ill, third, healthy, and fourth, chronic carriers, the striking discrepancy noted between the prevalence of cases in small, sparsely populated rural communities and the more thickly populated towns and cities at once disappears.

To sum up the aspect of the subject concerning the mode of infection, we may now state emphatically that the indications are all in

favor of personal communication of the virus. Hence the measures which we seek to put into effect against the introduction and spread of epidemic poliomyelitis should now be based on the conception of the personal factor as paramount, and not on the notion of insect carriage.

II

I turn now to the question of the nature of the virus or micro-organism causing epidemic poliomyelitis. You will recall that the virus is filterable, that is, it passes through the pores of earthenware filters which exclude under similar conditions the ordinary bacteria. We are now acquainted with a score or so of diseases in man and animals definitely proved or believed to be caused by parasites belonging to this filterable class. It is selfevident that these parasites are very minute; and because of their minuteness it has until recently been doubted whether they had actually been viewed under the microscope.

About two years ago, Dr. Noguchi and I announced that cultures of a very minute organism had been obtained which might be regarded as the possible microbic agent of epidemic poliomyelitis. The cultures were derived from the central nervous organs of human beings and monkeys who had had poliomyelitis. As evidence of the nature of the cultures it could then be stated that experimental poliomyelitis had been produced in monkeys by inoculation of the cultures. We have recently confirmed this result in an interesting manner. The culture employed for inoculation had been isolated about eighteen months before and had gone through a number of generations in artificial mediums. It was cultivated finally in a mixture of ascitic fluid and broth, and the fluid carrying large numbers of the micro-organisms—which are of extremely minute size—was injected, in some cases intraspinally, in others intraperitoneally into rhesus monkeys. The injection produced no immediate effect; indeed, a single injection caused no effect whatever. But when the intraperitoneal and intraspinal injections were repeated three or four times, the animals developed paralysis, and the paralyzed animals showed the peculiar histologic changes of the central nervous system indicative of poliomyelitis. In other words, these experiments showed that a culture of the microorganism mentioned, long removed from the nervous tissues, is capable of causing infection of monkeys, and that by this means the symptoms and lesions of epidemic poliomyelitis are produced.

The fact that several inoculations of the culture were required to cause infection agrees with observations previously made by Lewis and myself, that when a subminimal dose of the usual virus of poliomyelitis is injected into monkeys, no effect is produced; but when the subminimal injections are repeated, paralysis may suddenly supervene. The two sets of observations are, therefore, in accord.

SUMMARY

The data which I have had the pleasure of laying before you have led me to believe, first, that the microbic agent of epidemic poliomyelitis is present in the nasal and buccal secretions and is carried by persons, not insects, and communicated by them in such manner as to gain access to the upper respiratory mucous membranes of other persons, among whom a portion, being susceptible to the injurious action of the virus, acquire the infection and develop the disease.

The clinical variety or form of the disease which they develop may be the frankly paralytic, the meningitic, or the abortive and ambulatory in which no severe symptoms whatever appear. But however the persons may be affected, they become potential agents of dissemination of the virus of poliomyelitis, as do a number of healthy persons who have been in intimate contact with those who are ill, and another group of persons who have recovered from an acute attack of poliomyelitis. These several classes of infected or contaminated persons constitute the active means through which the virus is spread and to the control of which sanitary measures designed to prevent epidemics must be directed.

Finally, the virus or microbic agent of epidemic poliomyelitis appears now to have been cultivated and to consist of minute globular bodies, capable of being distinctly viewed under the high powers of the microscope.

LEUKOCYTE COUNTS DURING DIGESTION IN BOTTLE-FED INFANTS *

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It is the consensus of opinion, or belief of the majority of writers, that one of the physiologic causes of leukocytosis is digestion, or ingestion of food. It is the purpose of this paper to show that such is not constantly the case — at least in bottle-fed infants. Most of the text-books speak of physiologic leukocytosis. Some of the standard works on pediatrics state this leukocytosis to be more pronounced in children; a few speak of its being inconstant; and many ignore it entirely.

Yet it is very important whether this is, or is not, the case, especially in the interpretation of the leukocyte count in pathologic conditions.

REVIEW OF THE LITERATURE

The most striking thing in reviewing the literature on the subject is the fact that physiologic variations in leukocytes are seldom taken into account when drawing conclusions in a comparison of counts. Occasionally an attempt to avoid the disturbing factor of digestive leukocytosis in comparative counts is made,¹ for instance, by taking counts from three to five hours after a meal. The fallacy of this will become clear later on.

The first research in digestive leukocytosis was by Moleschott² in 1854. Following his work came that of Hirt³ in 1856; Malassez⁴ in 1876; Halla⁵ in 1883; Reinecke⁶ in 1883. These are all of interest historically, but as practical researches they do not stand because of poor methods of counting and small number of cases.

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1. Orr: Leukocyte and Differential Counts in Ward and Open Air Treatment, *Am. Jour. Med. Sc.*, 1912, cxliv, p. 238.

2. Moleschott: Ueber das Verhältniss der farblosen Blutkörperchen zu den farbigen in den verschiedenen Zuständen des Menschen, *Wien. med. Wchnschr.*, 1854, No. 8, p. 113.

3. Hirt: Ueber das numerische Verhältniss zwischen den weissen und roten Blutkörperchen, *Arch. f. Anat. u. Physiol.*, 1856, p. 174.

4. Malassez: *Gaz. méd. de Paris*, 1876, No. 25, p. 297.

5. Halla: Ueber den Hämoglobingehalt des Blutes, etc., *Ztschr. f. Heilk.*, 1883, iv, 198.

6. Reinecke: Ueber den Gehalt des Blutes an Körperchen, *Virch. Arch. f. path. Anat.*, 1889, cxviii, 148.

In 1892, Rieder⁷ found that seventeen of twenty-five adults gave digestive leukocytosis, and eleven of twelve children; and that the children showed a higher or stronger leukocytosis than adults. He counted before, and only three hours after the midday meal, however, and counted few cells.

In 1892, Schwinge⁸ carried out a small research on two adults and two children, examining the blood at two-hour intervals, and concluded that children showed more digestive leukocytosis than adults.

In 1898, Gregor,⁹ in nine researches on healthy children, did not always find leukocytosis; very little in breast-fed children, and then only after many hours. In eight of fifteen babies with chronic injury of bowel function he found a distinct leukocytosis with protein supply. He concluded that it is not clear why one child has and another has not digestive leukocytosis; that in most cases after a hunger period protein food causes leukocytosis; that the maximum count is at the noon hours and after the chief meal.

In 1900, Japha¹⁰ examined fourteen reasonably bowel healthy children of whom eight showed at some time after the meal a higher leukocytosis than before. Of these eight, three could be ruled out because of complications, or great irregularity in the counts, leaving only five of the fourteen. He concluded that one must not call every leukocytosis after a meal a digestive leukocytosis, as variations exist regardless of meals; that his work and that of others before him did not prove a digestive leukocytosis; that digestion and assimilation did not hang together; that as leukocytosis was not present under normal conditions one could not make any differential diagnosis in chronic dyspepsia and enteritis.

The same author¹¹ in 1901, in a few carefully made researches on his own person, came to the conclusion that adults showed a digestive leukocytosis in a limited sense, in that it occurred after the noon meal, at which time there was a periodical increase of the white blood cells regardless of food. He further stated that the rise was not constant and was hindered by constipation. The increase was mostly in the polymorphonuclear cells.

7. Rieder: Beitrag zur Kenntniss der Leukocytosis und verwandter Zustände des Blutes, Leipsic, 1892, F. C. W. Vogel.

8. Schwinge: Ueber den Hämoglobingehalt, etc., Arch. f. d. ges. Physiol., 1898, lxxiii, 299.

9. Gregor: Untersuchungen über Verdauungs-Leukocytose bei magendarmkranken Säuglingen, Arch. f. Verdauungskrankh., 1898, iii, 387.

10. Japha: Die Leukocyten beim gesunden und kranken Säugling, Jahrb. f. Kinderh., 1900, p. 242.

11. Japha: Ueber Verdauungs-Leukocytose, Deutsch. Aerzt., Zeitung, 1901, iii, 145.

In 1904 Moro¹² examined seven children. He found that digestive leukocytosis was inconstant, although it did occur on the first cow's milk meal to a breast-fed baby, and he considered this a reaction against foreign protein.

In 1911 Wernstedt¹³ examined about twenty-seven children. He found that the curves of leukocytes resembled irregular fever curves regardless of whether the infant was fed breast milk, boiled breast milk, cow's milk, or whether it was the first meal of a new-born baby. His charts show that the average of counts after meals were seldom higher than before. He believed that rest or motion, sleep or wakefulness had considerable influence on the count, and his highest counts were on crying children and the lowest on those in sleep or rest.

There have been many researches to determine the cause of digestive leukocytosis.

Hofmeister¹⁴ found that in the intestine of a cat under the influence of food the lymph cells rose in number and that the lymph vessels filled. This was chiefly in the stomach and upper small intestine. Heidenhain,¹⁵ however, thought that in the thoracic duct the cells were too few and the chyle protein too small in amount to account for the supply in the body.

Pohl,¹⁶ in fifty trials on a dog, always obtained digestive leukocytosis (with three exceptions) when protein food was given. He claimed from his examinations that the intestinal veins were richer in white blood cells than the arteries, and believed this to be the source of the cellular increase after the ingestion of food.

Rieder⁷ could not demonstrate this, and thinks the increase is due to a chemotaxis phenomenon, the digestive products in the blood causing an attraction.

Müller¹⁷ found that a prolonged hunger period followed by a protein rich meal gave leukocytosis. Burian and Schur¹⁸ also found that an eighteen-hour hunger period followed by a protein meal caused

12. Moro: Vergleichende Studien über die Verdauungsleukocytose beim Säugling, *Arch. f. Kinderh.*, 1904, xl, 39.

13. Wernstedt: Bidrag till fragen förekomsten af en digestion Leukocytos, etc., *Nord. med. Ark.*, Stockholm, 1910, 3, f, afd. ii, No. 6, p. 1.

14. Hofmeister: Ueber Resorption und Assimilation der Nährstoffe, *Arch. f. exper. path. u. Pharmacol.*, 1886-7, xxii, 306.

15. Heidenhain: Beiträge zur Histologie und Physiologie der Dünndarmschleimhaut, *Arch. f. d. ges. Physiol.*, 1888, xliii, supplement, p. 1.

16. Pohl: Ueber Resorption und Assimilation der Nährstoffe; Die Vermehrung der farblosen Zellen im Blute nach Nahrungsaufnahme, *Arch. f. exper. Path. u. Pharmacol.*, 1889, xxv, 31.

17. Müller: Klinische Beobachtungen über Verdauungs-Leukocytose, *Prag. med. Wchnschr.*, 1890, xv, 213, 228, 239.

18. Burian und Schur: Verdauungsleukocytose und Verdauung, *Wien. klin. Wchnschr.*, 1897, x, 137.

leukocytosis. They could find no relation to nitrogen excretion, and believed the phenomenon not to be one of resorption, but a reaction against injurious foodstuffs.

The results of von Limbeck¹⁹ were similar to those of Burian and Schur, and he also thought constipation hindered the result.

Reinert²⁰ from his examinations came to the conclusion that the lowest count of the day was in the morning (six to ten), and the highest about four in the afternoon. He thought food made very little difference.

Goodall, Gulland and Paton²¹ in 1903, and Goodall and Paton²² in 1905 did considerable work on dogs and cats. During the course of digestion they simultaneously examined the blood from the mesenteric veins and arteries, and the bone marrow. Their conclusions were that leukocytosis was present after meals, its maximum being at about four hours; that it was both a polymorphonuclear and a lymphatic increase; that the number and variety of cells were the same in the mesenteric arteries and veins, but much increased in the blood from the bone marrow; and they considered this to be the source of the increased number of cells in the blood during digestion. Removal of the spleen did not hinder the production of leukocytosis.

Finkelstein²³ believed it was the whey content and not the protein which determined the production of leukocytosis during digestion. So also Rosenstern,²⁴ who believed the rise in cells was a reaction analogous to the fever reaction in ingestion of sugar and salts. He examined only ten children, and made his counts only about three to five times a day.

It is interesting to note that Argand and Billard²⁵ found in examining two rabbits that starvation caused a leukopenia with mononuclear cells predominating which quickly returned to normal on feeding.

19. Von Limbeck: *Klinisches und Experimentelles über die Entzündliche Leukocytose*, Ztschr. f. Heilk., 1889, x, 392.

20. Reinert: *Die Zählung der Blutkörperchen und ihre Bedeutung für die Diagnose und Therapie*, Leipsic, 1891, F. C. W. Vogel.

21. Goodall, Gulland and Paton: *Digestive Leucocytosis in Normal and in Spleenless Dogs*, Jour. Physiol., London, 1903, xxx, 1.

22. Goodall and Paton: *Digestion Leucocytosis, Source of the Leucocytes*, Jour. Physiol., London, 1905, xxxiii, 20.

23. Finkelstein: *Verhandlungen der Gesellschaft für Kinderheilkunde*, 1906, xxiii, 160.

24. Rosenstern: *Ueber alimentäre Leukocytose*, Monatschr. f. Kinderh., Leipsic, 1909, viii, 9.

25. Argand and Billiard: *Inversion de la formule leucocytaire sous l'influence de l'inanition*, Compt. rend. Soc. de Biol., Paris, 1911, lxx, 146.

Richet,²⁵ in working on a dog, found that uncooked albuminoid matter produced leukocytosis, and cooked did not, even in enormous doses. He concluded that the reaction was due to certain albuminoid substances escaping the action of the digestive juices and entering the blood.

This review of the literature contains most of the original work done on the subject. It does not contain all, as some of the articles were not accessible. It is enough, however, to give us the ideas of the majority of authors and researchers, which may be summarized as follows:

1. In babies digestive leukocytosis is inconstant.
2. In adults digestive leukocytosis is inconstant.
3. A rise occurs in the early afternoon regardless of food.
4. Animals such as dogs, cats and rabbits do show a leukocytosis after food high in protein.
5. The majority of researchers think protein food to be necessary for the production, and a few think the whey and sugar content to be the cause.

It is significant that much of the work has been done on animals.

OBSERVATIONS ON FIFTY CHILDREN

The present report consists of a study of fifty children, on whom over seven hundred blood counts were made.

The method of study pursued was to take a leukocyte count immediately before feeding, immediately after feeding, fifteen minutes after feeding, one-half hour after, one hour after, one and a half hours after, and so on every half-hour until the next feeding. These groups of blood counts (beginning before one feeding, and ending before another) are taken to constitute a "series" and will be spoken of as such. There are 120 of these "series" in this report.

The leukocytes were counted with the low power; four smears were made on the Jappert-Ewing counting chamber; and the contents of two large squares counted on each, making a total of eight large squares.

All matters of technic were carefully watched, and the same pipette and counting chamber used during a series. The toes were found to be the most convenient part of the anatomy for the removal of blood. As far as possible the same amount of pressure was used in extracting blood, and all causes of local congestion avoided. For example, instead of using one toe during a series, different toes were used.

26. Richet: *La réaction leucocytaire: digestion, etc.* Presse. méd., 1913, xxi, 539.

The infants on whom this study was made were all bottle-fed, and, while not exactly normal children, were of the type usually seen in a hospital ready for discharge. They were practically all somewhat underweight for their age. With one or two exceptions they could be classed under three groups: "Convalescent Pneumonia," "Convalescent Gastro-Enteritis" and "Feeding." Eight of these babies were examined during one feeding period only, but all the rest had two or more series made, some running as high as twelve or thirteen.

The results of the analysis of these cases are interesting, in that physiological leukocytosis after feeding was not found in most instances, and the opposite condition of leukopenia prevailed. A single rise in leukocytosis after a meal was not considered a digestive increase unless it persisted, as it may be due to other causes. As pointed out by Wernstedt,¹³ it may be the result of crying or great muscular activity. Also in judging of the increase or decrease, the mean of the counts after the meal (that is, during the series) was compared to the count before the meal. As examples of what the extraneous sources of increased leukocyte count may be, see illustrative cases—6, 7, 8 and 9. These cases show that striking a small artery, crying, cold extremities necessitating much pressure to extract the blood, and getting the blood from a place previously punctured, may be the causes of increased leukocyte counts. When such factors as these could be determined, the increase in leukocyte count was not taken to be a digestive one. The frequency with which such things occurred may be judged by the fact that if these were not carefully ruled out, seventy-five of the 120 series would show an increased count during the digestive period, instead of the forty-four (or 28.3 per cent.) shown below.

Of the fifty children, only six, or 12 per cent., constantly showed an increase in the white blood cells during digestion, although sixteen, or 32 per cent., showed at times an increase, and at others a decrease. Contrasted with this, twenty-eight, or 56 per cent., constantly showed a decrease in leukocytes during digestion.

In considering the 120 series, 28.3 per cent. showed leukocytosis and 68.3 per cent. leukopenia. The remaining 3.3 per cent. were so irregular as to be undeterminable.

A study of Charts 1 and 2 will show the amount of leukopenia and when it occurs. The charts represent a summary of the fourth- and third-hour cases, respectively.

The curves, while irregular, clearly show the drop which in fourth-hour cases is greatest at one hour and reaches over 9 per cent., and in the third-hour cases is greatest between one and a half to two and a half hours, and reaches over 11 per cent.

SUMMARY OF CASES

| No. | Diagnosis | Age in Months | Gaining + Losing — | Stools During 1 day | Food | Average Count of Series | Time of Count | After Food, Leukocytosis + Leukopenia — |
|-----|---|---------------|-----------------------|--|---|-------------------------------|---------------------|---|
| 1 | Slight enteritis Underweight. | 8 | + | Three to six greenish-yellow, soft; few curds. | Caseln milk, 3.7-1.6-3, 4 oz. | 14,325 | 9-12 a. m. | — |
| ? | Normal except for slight anemia. | 14 | — | One formed yellow..... | Caseln milk, 3.7-1.6-3, 4 oz. | 17,020 | 9-12 p. m. | — |
| 3 | Normal convalescent gastro- enteritis. | 8 | + | Two soft yellow..... | 4-4.5-3.5. Whole milk, 8 oz. | 13,700 | 9-12 a. m. | + |
| | | | | | 4-4.5-3.5. Whole milk, 8 oz. | 13,460 | 9-12 p. m. | + |
| 4 | Normal convalescent slight gastro-enteritis. | 10 | + | Two soft yellow, with few curds, yellow, with few curds. | 2.6-3-2.3, 7½ oz. | 12,025 | ? | + |
| | | | | | 2.6-3-2.3, 7½ oz. | 11,960 | ? | + |
| | | | | | ¾ milk, 4 oz. | 15,500 | 9-12 a. m. | — |
| | | | | | ¾ milk, 4 oz. | 12,990 | 9-12 a. m. | — |
| | | | | | ¾ milk, 4 oz. | 13,725 | 1-4 p. m. | — |
| 5 | Feeding Later developed pertussis. | 4 | Stationary | Three soft yellow..... | 2.6-2, 3 oz. | 15,090 | 9-12 p. m. | + |
| | | | | | 3-6-2, 4 oz. | 21,450 | 3-6 p. m. | — |
| 6 | Normal convalescent gastro- enteritis.. | 4 | + | Soft yellow Constipated, greenish- yellow. | ¾ milk and 3% sugar, 5½ oz. | 14,160 | 9-12 p. m. | + |
| | | | | | 3-6-2.5, 5½ oz. | 18,420 | 9-12 a. m. | — |
| 7 | Feeding Convalescent from sugar injury. | 7 | + | One soft yellow..... One soft yellow..... | Caseln milk with cream, 5 oz., 3.6-1.7-3.04 Caseln milk with cream, 5½ oz., 3.6-1.7-3.04 | 13,700 | 9-12 a. m. | — |
| | | | | | | 15,110 | 12-3 p. m. | + |
| 8 | Feeding | ½ to 1½ | Stationary | Two greenish-yellow, with fine curds. | 2.5-4-1.5, 2 oz. | 14,990 | 11-1 a. m. | — |
| | | | Stationary | Two greenish-yellow, with fine curds. | Whey, cream, 1.3-5.2-1.2 | 18,160 | 11-1 a. m. | — |
| | | | Stationary | Three greenish-yellow with fine curds | Whey, cream, 1.7-5-1.2, 2½ oz. | 14,880 | 11-1 a. m. | — |
| | | | + | Four soft brown..... | 2-7-2, 3½ oz. malt soup | 15,050 | 11-30 a. m.-2 p. m. | — |
| | | | + | Four soft brown..... | 2-7-2, 3½ oz. malt soup | 15,040 | 2-4:30 p. m. | — |
| 9 | Feeding | 3 | Stationary | One loose greenish-yellow, with fine curds. | ½ milk and 2% dextro maltose, 4 oz. | 15,290 | 9-12 a. m. | + |
| | | | Stationary | One loose greenish-yellow, with fine curds. | ½ milk and 2% dextro maltose, 4 oz. | 14,570 | 12-3 p. m. | + |
| 10 | Normal convalescent from gastro-enteritis. | 8½ | + | Three soft yellow..... | 3-6-3, 7½ oz. | 18,250 | 9-12 a. m. | — |

| | | | | | | | | |
|----|--|----|------------|---|--|--------|------------|------------------|
| 11 | Normal | 20 | Stationary | One formed yellow. | Whole milk, 8 oz. | 9,660 | ? | — |
| 12 | Normal convalescent from gastro-intestinal indigestion | 8½ | + | One formed yellow. | Whole milk, 8 oz. | 13,750 | ? | — |
| 13 | Normal convalescent pneumonia, developed pertussis. | 24 | + | Four soft yellow. | 4.5-4.4-2.57, 7 oz., whey, cream. | 12,470 | 9-1 a. m. | — |
| | | | | Four soft yellow. | 3-6.5-2.7, 7 oz., milk mixt. | 11,500 | 1-5 p. m. | — |
| | | | — | 0 | Whole milk, 8 oz. | 8,570 | 9-12 p. m. | — |
| | | | Stationary | 0 | Whole milk, 8 oz. | 10,620 | 9-1 a. m. | — |
| | | | Stationary | 0 | Cream wheat, 1 saucerful | 10,660 | 3 p. m. | — |
| | | | Stationary | 0 | Junket, 1 saucerful | 9,720 | 7 p. m. | — |
| | | | Stationary | 0 | Whole milk, 2 oz. | 8,800 | 9 p. m. | — |
| | | | Stationary | One soft yellow. | Whole milk, 8 oz., plus cream wheat. | 9,080 | 9-1 a. m. | + |
| | | | Stationary | One soft yellow. | Whole milk, 8 oz., plus toast. | 8,150 | 1-5 p. m. | + |
| | | | + | One soft yellow. | Whole milk, 5 oz., cream wheat. | 15,030 | 1-5 p. m. | ? (vaccillation) |
| | | | + | One soft yellow. | Whole milk, 8 oz. | 13,420 | 5-9 p. m. | — |
| | | | + | One soft yellow. | Whole milk, 8 oz. | 15,140 | 9-12 p. m. | + |
| | | | Stationary | 0 | Oatmeal, 1 saucerful | 18,530 | 9-1 a. m. | — |
| | | | + | One loose greenish-yellow | Whole milk, 8 oz. | 16,380 | 9-12 p. m. | + |
| | | | | | Whole milk, 8 oz. | 18,400 | 1-5 p. m. | + |
| 14 | Normal convalescent pneumonia. | 24 | Stationary | One hard yellow. | ¾ milk, 8 oz. | 12,500 | 1-5 p. m. | — |
| | | | + | One soft yellow. | Whole milk, 7 oz. | 18,260 | 9-1 a. m. | + |
| | | | + | One soft yellow. | Whole milk, 8 oz. | 15,500 | 9-12 p. m. | — |
| | | | Stationary | One loose greenish-yellow, with fine curds. | Whole milk, 8 oz., and cream wheat. | 16,350 | 9-1 a. m. | — |
| 15 | Otitis media | 30 | Stationary | Two soft brown. | Whole milk, 8 oz. | 13,300 | 5-9 p. m. | — |
| | Gastro-intestinal tract O.K. | | Stationary | Two soft brown. | Whole milk, 8 oz. | 18,980 | 9-12 p. m. | — |
| 16 | Convalescent pneumonia | 15 | Stationary | Two pasty yellow. | Whole milk, 8 oz. | 18,040 | 1-5 p. m. | — |
| | | | + | Two soft greenish-yellow | Whole milk, 8 oz. | 17,780 | 1-5 p. m. | + |
| | | | | | Whole milk, 8 oz. | 18,650 | 9-1 a. m. | + |
| 17 | Gastro-intestinal indigestion Sugar in urine vomiting. Later cleaned up. | 7 | — | Three soft yellow. | 3-5.3-2.6, 3 oz., whey, cream. | 18,930 | 9-12 p. m. | — |
| | | | — | Two soft yellow, with fine curds. | 0.58-5-1.9, 8 oz., whey, skimmed milk. | 18,500 | 9-1 a. m. | — |
| | | | — | Two soft yellow, with fine curds. | 0.58-5-1.9, 8 oz., whey, skimmed milk. | 18,110 | 1-5 p. m. | + |
| | | | — | Two soft yellow, with fine curds. | 0.58-5-1.9, 8 oz., whey, skimmed milk. | 17,300 | 5-9 p. m. | — |
| | | | — | Two soft yellow, with fine curds. | 0.58-5-1.9, 8 oz., whey, skimmed milk. | 18,730 | 9-12 p. m. | + |
| 18 | Feeding, premature | 3½ | Stationary | Two soft yellow. | 2.7-2, 3½ oz. malt soup | 8,850 | 1-5 p. m. | — |
| | | | Stationary | Two soft yellow. | 2.7-2, 3½ oz. malt soup | 12,430 | 5-9 p. m. | — |
| | | | Stationary | Two soft yellow. | 2.7-2, 3½ oz. malt soup | 9,540 | 9-12 p. m. | — |

SUMMARY OF CASES Continued

| No. | Diagnosis | Age in Months | Gaining + Losing - | Stools During Day | Food | Average Count of Series | Time of Count | After Food, Leukocytosis + Leukopenia - |
|-----|---|---------------|-----------------------|---|---|--|--|---|
| 19 | Feeding | 8 | + | Three pasty yellow, with fine curds. Three pasty yellow, with fine curds. One pasty yellow..... | 3.5-5-3.5, 7 oz. 3.5-5-3.5, 7 oz. 3.5-5-3.5, 7 oz. | 10,870 9,880 11,560 | 9-12 p. m. 12- 3 p. m. 1- 5 p. m. | - - - |
| 20 | Bronchitis | 22 | + | One constipated yellow... | Oatmeal and whole milk, 5 oz. | 20,200 | 9- 1 a. m. | ? (vaccination) |
| | Gastro-intestinal tract nor- mal. | | + | One constipated yellow... | Egg and toast and whole milk, 8 oz. | 18,250 | 1- 5 p. m. | - |
| | | | + | One constipated yellow... | Junket, whole milk, 3 oz. | 22,400 | 5- 9 p. m. | ? (vaccination) |
| 21 | Gastro-intestinal indigestion | 15 | + | Four soft greenish-yellow, with fine curds. Three soft yellow..... Three soft yellow..... | 2.7-3.1-2.5, 8½ oz., milk and soy bean. 2.7-3.1-2.5, 8½ oz., milk and soy bean. 2.7-3.1-2.5, 8½ oz., milk and soy bean. | 15,400 12,700 13,860 | 1- 5 p. m. 9- 1 a. m. 1- 5 p. m. | - - + |
| | | | + | One soft yellow, with file curds. One soft yellow, with file curds. One pasty dark green.... One pasty dark green.... One soft brown, with fine curds. | 3.13-3.9-2.8, 8 oz., milk, soy bean. 3.13-3.9-2.8, 8 oz., milk, soy bean. 2.5-1.5-2, 6 oz., casein milk 2.5-1.5-2, 6 oz., casein milk 2.7-2, malt soup..... | 14,540 14,230 16,300 17,120 23,940 | 9- 1 a. m. 1- 5 p. m. 1- 5 p. m. 9-12 p. m. 9-12 p. m. | + |
| 22 | Feeding, tuberculosis (?).... | 19 | + | One soft yellow..... | Whole milk, 6 oz. | 11,400 | ? | - |
| 23 | Normal convalescent gastro- enteritis. | 5 | Stationary | Two soft yellow..... | % milk and 3% dextro maltose, 5 oz. | 16,630 | 9-12 a. m. | - |
| 24 | Feeding | 8 | Stationary | Two soft yellow, with casein curds. Two soft yellow, with casein curds. | 2.5-5-2.5, 6 oz. 2.5-5-2.5, 6 oz. | 10,160 9,880 | 9-12 a. m. 12- 3 p. m. | - - |
| 25 | Feeding | 5 | Stationary | Two loose brown, with mucous. Two loose greenish-yellow | Water, 5 oz. No food | 7,960 9,950 | 9-12 a. m. 9-12 a. m. | - - |
| 26 | Feeding | 7½ | Stationary | Three pasty yellow, with fine curds. Three pasty yellow, with fine curds. | % milk, 6 oz. % milk, 6 oz. | 12,310 12,720 | 9-12 a. m. 12- 3 p. m. | + |

| | | | | | | | | |
|----|-------------------------------|-----|------------|--|--|----------------------------|--|---|
| 27 | Convalescent enteritis | 5 | — | Two soft greenish-yellow, with some mucus. Two soft greenish-yellow, with some mucus. Three soft yellow..... | % milk and 2% dextro maltose, 4 oz. % milk and 2% dextro maltose, 4½ oz. % milk and 2% sugar, 4½ oz. | 11,600 11,300 17,150 | 9-12 a. m. 12-3 p. m. 9-12 a. m. | — — — |
| 28 | Feeding | 3 | Stationary | Three spongy yellow..... | ½ milk and 3% dextro maltose, 3½ oz. | 10,600 | 9-12 a. m. | — |
| 29 | Feeding | 5½ | — | Three soft yellow, with fine curds. Three soft yellow, with fine curds. | % milk and 3% dextro maltose, 5 oz. % milk and 3% dextro maltose, 5 oz. | 5,940 5,760 | 9-12 a. m. 12-3 p. m. | + — |
| 30 | Feeding | 4½ | — | One soft yellow, with fine curds. Two soft yellow..... | 2.5-1.4-3, 5½ oz., casein milk. 2.5-1.4-3, 6½ oz., casein milk. | 91,200 13,140 | 9-12 a. m. 9-12 a. m. | + + |
| 31 | Feeding | 8 | — | Three loose yellow, with fine and casein curds. Four loose greenish-yellow, with fine curds. | ¾ milk, 6 oz., boiled.... 2.5-2, 4 oz. | 14,980 31,470 | 1-5 p. m. 9-12 a. m. | + — No apparent reason for high count. |
| 32 | Slight gastro-enteritis | 7½ | + | Two loose greenish, with mucus. | ½ milk and 3% dextro maltose, 5 oz. | 8,820 | 9-12 a. m. | — |
| 33 | Feeding | 6 | — | Two loose yellow | Buttermilk, 5 oz. | 11,800 | 9-12 a. m. | + |
| 34 | Convalescent gastro-enteritis | 14 | + | Two loose yellow..... Two loose yellow..... | Buttermilk, 5 oz. 2.5-3.5-3, casein milk and dextro maltose, 5½ oz. 2.5-3.5-3, casein milk and dextro maltose, 5½ oz. | 13,980 6,350 6,420 | 9-12 a. m. 9-12 a. m. 12-3 p. m. | — — — |
| 35 | Feeding | 15½ | + | One constipated yellow.. | % milk, 5 oz. | 13,400 | 9-1 a. m. | — |
| 36 | Convalescent gastro-enteritis | 7½ | + | Two soft yellow..... Two soft yellow..... | ½ milk and soy bean, 6 oz. ½ milk and soy bean, 6 oz. | 8,810 8,070 | 9-1 a. m. 1-5 p. m. | — + |
| 37 | Convalescent gastro-enteritis | 8 | Stationary | One loose greenish-yellow | 2.6-3, 8 oz. | 23,800 | 9-1 a. m. | + No apparent reason for high count. |
| 38 | Convalescent gastro-enteritis | 7 | Stationary | One loose greenish-yellow Two soft whitish, with fine curds. Three soft whitish, with fine curds. | 2.6-3, 8 oz. % milk, 6 oz. % milk 5½ oz. | 20,550 11,450 9,100 | 1-5 p. m. 1-5 p. m. 1-5 p. m. | + — — |

SUMMARY OF CASES. Continued

| No. | Diagnosis | Age In Months | Gaining + Losing - | Stools During Day | Food | Average Count of Series | Time of Count | After Food, Leukocytes + Leukopenia - |
|-----|---|---------------|-----------------------|--|---|-------------------------|--------------------------|---------------------------------------|
| 39 | Convalescent gastro-enteritis. Slight bronchitis. | 6 | - | Two soft greenish-yellow, with fine curds. Two soft greenish-yellow, with fine curds. | 2.5-12.2, 2 oz. 2.5-4.2-2, 2 oz. | 14,790 16,400 | 9-1 a. m. 1-5 p. m. | - + |
| 40 | Normal | 15½ | + | Two pasty yellow..... | Whole milk, 8 oz. | 10,220 | 9-1 a. m. | + |
| 41 | Normal | 26 | ? | ? | Whole milk, 8 oz. | 16,080 | 1-5 p. m. | - |
| 42 | Feeding | 17 | + | One loose yellow..... One soft yellow..... | ¾ milk, 5 oz. ¾ milk, 5 oz. | 10,870 10,680 | 1-5 p. m. 1-5 p. m. | - - |
| 43 | Feeding | 11½ | Stationary | Three pasty greenish-yellow. low. | Buttermilk, 4 oz. | 5,870 | 9-1 a. m. | - |
| 44 | Feeding Convalescent essential edema. | 19½ | + | Two constipated yellow.. | Whole milk, 7½ oz. | 8,070 | 9-1 a. m. | - |
| 45 | Feeding | 7½ | Stationary | Two loose greenish-yellow, with casein curds. Three constipated yellow | ½ milk and soy bean... No food | 16,890 16,850 | 9-1 a. m. 1-5 p. m. | - - |
| 46 | Convalescent enteritis..... | 11 | Stationary | Two soft yellow..... | ¾ milk and 2% dextro maltose, 8 oz. | 9,840 | 9-1 a. m. | - |
| 47 | Feeding | 3 | + | Soft yellow Soft yellow | No food 7, i. e., food unknown... | 15,260 14,400 | 9-12 a. m. 9-12 a. m. | - - |
| 48 | Feeding Convalescent gastro-enteritis. | 9½ | + | Three soft yellow..... Three soft yellow..... | ¾ milk, 7 oz. ¾ milk, 7 oz. | 14,920 13,930 | 9-1 a. m. 1-5 p. m. | - - |
| 49 | Feeding Bronchitis. | 5 | Stationary | Three loose greenish-yellow. low. | ¾ milk, 4 oz. | 12,640 | 9-12 a. m. | - |
| | | | Stationary | Three loose greenish-yellow. low. | ¾ milk, 4 oz. | 13,760 | 9-12 a. m. | - |
| 50 | Normal convalescent enteritis. | 7 | Stationary | Two soft yellow, with fine curds. | 2.5-4-2, 7 oz. | 13,430 | 9-1 a. m. | - |
| | | | Stationary + | Two soft yellow, with fine curds. Two soft yellow..... | 2.5-4-2, 7 oz. No food | 10,270 9,260 | 1-5 p. m. 9-1 a. m. | - - |

The explanation of the fall after the third hour in Chart 1 lies in the fact that this curve, being a composite one of all fourth-hour cases, represents series taken at different times of the day. If we take into consideration the fact that the highest count of the day is before the morning feeding, we have a ready explanation of this peculiar fall.

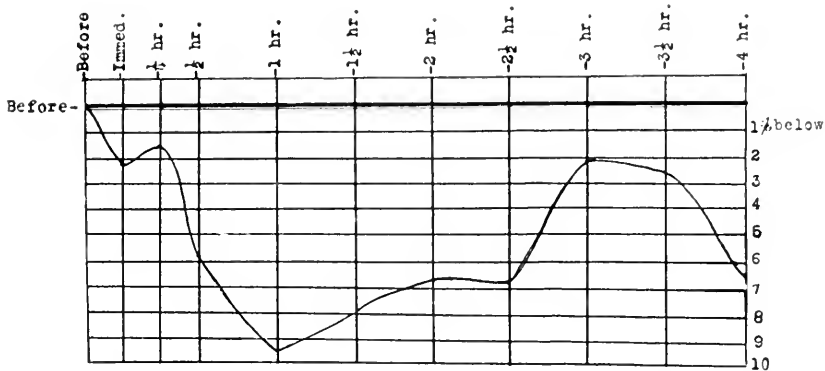


Chart 1.—Fourth-hour cases. In this and the following chart the vertical lines represent time and the horizontal percentages.

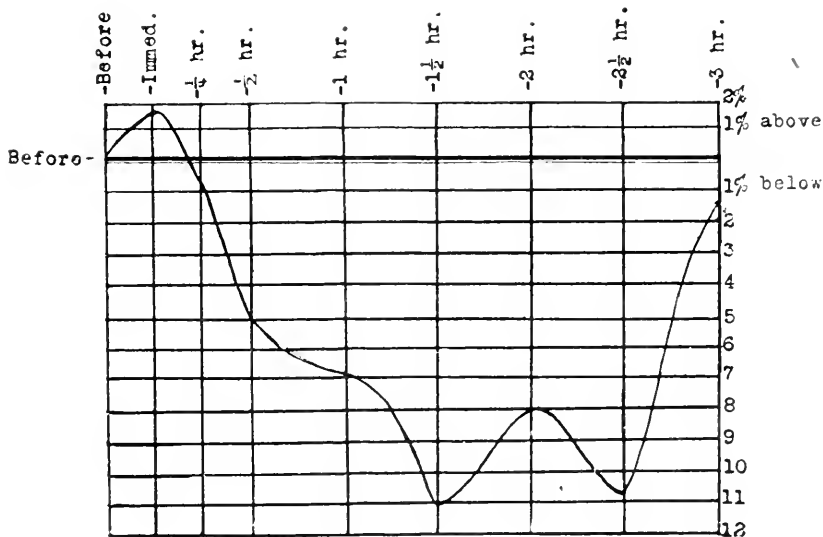


Chart 2.—Third-hour cases.

As this is not marked until about four or five hours after the first morning feeding, it affects the third-hour cases but little. This does not correspond to the findings of Gregor,⁹ Japha¹¹ and others. Of twenty-two cases in the present report which were studied both in morning and afternoon, however, ten showed a higher average of

counts in the morning, eight showed about the same both morning and afternoon, and only four showed a higher average of counts in the afternoon.

Age.—The patients varied from 3 weeks to 26 months in age. No relation of digestive leukocytosis or leukopenia could be established according to age grouping.

Nature of Food.—The majority of the patients were fed on cow's milk mixtures, although a few had casein milk, malt soup, whey and cream, and buttermilk mixtures. The number of patients fed on other than cow's milk mixtures was too small to permit judgment of their relation to leukocytosis or leukopenia.

Temperature.—No relation between leukocytosis and leukopenia, and temperature could be established.

Gain or Loss in Weight.—Of the 120 series at the time of counting, fifty-six, or 46.66 per cent., were gaining in weight; nineteen, or 15.83 per cent., were losing, and forty-five, or 37.5 per cent., were stationary in weight. The proportions of these three groups showing digestive leukocytosis or leukopenia may be shown in the following tabulation:

| | Leukocytosis Per Cent. | Leukopenia Per Cent. | No Change or Vacillation Obscured Per Cent. |
|------------------------------|---------------------------|-------------------------|---|
| Gaining (56 series)..... | 26.78 | 66.07 | 7.14 |
| Losing (19 series) | 47.36 | 52.63 | 0 |
| Stationary (45 series) | 22.22 | 75.55 | 2.22 |

Briefly, then, these percentages show that leukocytosis during digestion occurred about twice as frequently in children losing weight as in those gaining or stationary, and that leukopenia is somewhat more constant in children gaining or stationary than in those losing weight.

Time of Day.—The relation to the time of day is shown in the following tabulation:

| | Leukocytosis Per Cent. | Leukopenia Per Cent. | No Change Per Cent. |
|--|---------------------------|-------------------------|------------------------|
| Morning or first feeding (51 series) | 27.45 | 68.62 | 3.92 |
| Early afternoon or second feeding (39 series) | 33.33 | 64.1 | 2.56 |
| Late afternoon or third feeding (8 series) | (All showed leukopenia) | | |
| Last feeding or 9 p. m. feeding (18 series) | 27.7 | 66.6 | 5.5 |

There does not, therefore, seem to be much relation to the time of day, unless we consider the small number of series taken during the late afternoon feeding.

ILLUSTRATIVE CASES

The counts do not show a regular progressive decrease or increase as the case may be, but are often quite changeable and variable.

For example:

CASE 1.—Showing counts taken during four-hour period, the child receiving no food for several hours before or during the series.

At 9 a. m., white blood cells, 11,000; 9:30 a. m., 10,150; 10 a. m., 9,300; 10:30 a. m., 7,925; 11 a. m., 10,575; 11:30 a. m., 8,540; 12 noon, 7,725; 1 p. m., 8,900. This same child had shown on two other occasions a leukopenia following ingestion of food.

CASE 2.—A child convalescent from acute gastro-enteritis. He is now 13 months old, having normal temperature, and one or two firm, yellow bowel movements a day. Showing leukopenia.

At 9 a. m., white blood cells were 8,475; at 9:02 he was given 5½ ounces of casein milk with 2 per cent. sugar added (2.5-3.5-3); he finished his bottle at 9:15, and blood taken at that time showed a count of 5,875; a quarter of an hour later, white blood cells 6,825; half an hour later, 5,350; one hour, 4,900; one and one-half hours, 6,225; two hours, 5,475; two and one-half hours, 7,125; three hours, 7,275.

CASE 3.—The patient is a child of 1 year, convalescent from an acute gastro-intestinal upset. He is now gaining and having good stools.

At 9:20 a. m., his leukocytes were 6,600; at 9:24, he was given a buttermilk mixture of which he took 4 ounces, and finished this at 9:32. At that time his leukocytes were 5,800; a quarter of an hour later they were 5,700; half an hour, 6,150; one hour, 5,600; one and a half hours, 5,000; two hours, 5,950; two and one-half hours, 5,800; three hours, 6,800; three and three-fourth hours, 5,250.

CASE 4.—A child of 20 months, whose diagnosis was essential edema, but who at the present time is an entirely normal child.

Before his feeding of 7½ ounces of whole milk, his leukocytes were 9,550; half an hour after finishing this bottle, they were 8,600; one hour, 6,600; one and a half hours, 7,360; two hours, 6,300; two and one-half hours, 8,060; three hours, 7,960; three and three-fourth hours, 10,130.

CASE 5.—A child of 8 months, who is not doing very well at the time of examination, as she is having loose, greenish-yellow bowel movements and is vomiting somewhat. She shows a distinct leukocytosis after food.

Before food her count was 18,625. She was fed 8 ounces of a 2-6-3 milk mixture, and immediately regurgitated a small amount. A quarter hour after food her white blood cells were 32,050; half an hour, 28,350; one hour, 25,500; one and a half hours, 24,300; two hours, 23,650; two and one-half hours, 25,800; three hours, 21,850; three and one-half hours, 19,200; four hours, 18,700.

CASE 6.—Showing effect of cold. Before food, 16,675. Fed 6 ounces milk, 3 ounces soy bean gruel. One-half hour afterward, 13,825; one and one-half hours, 17,325 (toes very cold from exposure); two hours, 13,875 (toes warm again); three and one-half hours, 15,275.

CASE 7.—Showing the effect of removing blood from a puncture made some time previously. Before food, 10,425. Fed 6 ounces milk, 2 ounces soy bean gruel. Quarter hour afterward, 13,850; half an hour, 14,675; one hour, 14,400; two hours, 20,950 (blood removed from puncture made at one hour previously), three hours, 12,950.

CASE 8.—Showing the effect of crying. Before food, 10,250. Fed 8 ounces whole milk and two crackers; a quarter of an hour afterward, 9,125; half an hour, 12,000 (crying and struggling); one hour, 10,350; one and a half hours, 7,865; two hours, 9,525; two and one-half hours, 9,415; three hours, 10,600; three and one-half hours, 11,275; four hours, 10,475.

CASE 9.—Showing the effect of arterial bleeding. Before, 11,050. Fed 3-5-3 mixture, 8 ounces; a quarter of an hour afterward, 10,000; half an hour, 9,750; one hour, 10,500; one and a half hours, 12,300 (struck small artery in big toe); two hours, 8,800; two and one-half hours, 8,050; three hours, 8,250; three hours and fifty minutes, 8,700.

CASE 10.—Child showing distinct leukocytosis after ingestion of food. Before, 9,800. Fed $\frac{2}{3}$ milk, 6 ounces. Immediately after taking, 9,250; a quarter of an hour afterward, 11,600; half an hour, 10,500; three quarters of an hour, 12,300; one hour, 12,600; one and a half hours, 11,450; two hours, 12,100; two and one-half hours, 11,550; three hours, 11,600; three and one-half hours, 14,200; three and three-fourths hours, 9,900.

CASE 11.—Showing a child followed directly through morning and afternoon feedings, and having a slight but not continued rise after the second meal of the day. Before first morning feeding, 9 a. m., white blood cells, 12,700. Fed 3 ounces milk and 3 ounces soy bean gruel. Quarter hour afterward, 7,625; half an hour, 9,925; one hour, 7,100; one and a half hours, 8,600; two hours, 9,050; two and one-half hours, 7,975; three hours, 8,275; four hours, 8,050. Then fed 3 ounces milk and 3 ounces soy bean gruel. Immediately afterward the white blood cells were 9,025; half an hour afterward, 8,275; one hour, 7,500; two hours, 7,625; two and one-half hours, 7,925; three hours, 7,400; three and one-half hours, 7,350; four hours, 9,500.

A summary of the actual counts on uncomplicated cases shows the following figures for different ages:

| Age | Average | Minimum | Maximum | No. Counts |
|---------------------|---------|---------|---------|------------|
| 1-4 months | 13,870 | 8,850 | 15,290 | 78 |
| 4-8 months | 12,360 | 7,960 | 17,150 | 254 |
| 8-12 months | 12,290 | 9,880 | 15,500 | 115 |
| 12-18 months | 12,820 | 6,390 | 17,120 | 103 |
| 18-24 months | 10,720 | 8,070 | 13,750 | 21 |
| Over 24 months..... | 11,520 | 8,150 | 16,350 | 62 |

Remember these counts are on bottle-fed babies. Carstanjen,²⁷ in a number of counts, claims the average to be 12,500 in the first year. Rabinowitsch²⁸ thinks the counts usually given are too high, and says that healthy children from 1 to 16 years should average from 6,000 to 7,000.

CAUSE

As to why some children show leukocytosis and others leukopenia after food, and why the same child may show at times an increase and at times a decrease after food—this research offers no adequate explanation. Careful study of the cases as regards age, gain or loss in weight, character of stools, nature of food, temperature, and time of day did not show any definite relation. It might be added in this connection that six children were studied through a four-hour period,

27. Carstanjen: Wie verhalten sich die procentischen Verhältnisse der verschiedenen Formen der weissen Blutkörperchen beim Menschen unter normalen Umständen? *Jahrb. f. Kinderh.*, 1900, lii, 333.

28. Rabinowitsch: Die Leukocyten verschiedenen Altersstufen: Untersuchungen über die Leucocyten gesunder Kinder. *Arch. f. Kinderh.*, 1912, lix, 161.

beginning at 9 a. m., and received no food then or for several hours before. These all showed a gradually decreasing leukocyte count.

A theory which may be offered here is that ingestion of food, and beginning of the activities of the gastro-intestinal tract, both glandular secretion and muscular movement thus causing increased blood supply to the splanchnic area, may attract leukocytes away from the superficial blood, and result in a diminished number of cells when counted by the ordinary methods.

CONCLUSIONS

1. Bottle-fed babies do not constantly show digestive leukocytosis; in fact, the majority show a smaller number of leukocytes in the superficial blood after taking food than before.

2. This decrease is greatest at from one to two and a half hours after food, and tends to rise before the next feeding.

3. When a rise does occur, it is most frequently soon after feeding, and begins to decline in a half-hour.

4. Crying, struggling and chilling of the part from which the blood is extracted increases the count.

5. There seems to be as yet no adequate explanation for the increase or decrease.

6. Comparative counts should be made at the same time of day, and at the same time in relation to food.

I wish to thank Dr. J. C. Gittings and Dr. William Pepper for their valuable advice in the preparation of this work; Dr. Theodore LeBoutillier, Dr. John F. Sinclair and Dr. Arthur Newlin for their kindness in allowing me the use of their cases at the Babies' Hospital.

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THE INFLUENCE OF MENSTRUATION ON BREAST MILK *

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If one reviews the current literature as presented in the text-books on the effect of menstruation on breast milk he is struck with the fact that opinions are very diverse and that many statements are made without sufficient scientific foundation. In an endeavor to obtain scientific facts on this subject we quite carefully looked through the literature and were able to find only a few articles of any scientific value.

In 1853 Vernois and Becquerel¹ in three cases examined the milk secreted before and during menstruation. They found that taken as a whole there was a lower specific gravity with a decrease of water and sugar content and an increasing total solid and casein, while the fats and ash remained about the same during the menstrual period. But a closer inspection of their cases shows that while Cases 1 and 3 agreed with these findings, Case 2 showed opposite results and that whereas the average obtained was as above stated, the individual differences were such as to render the average findings of little value.

Very interesting to American physicians will be the fact that the next article, appearing in 1856, was by N. S. Davis.² His examination in one case showed a marked diminution of all the solid constituents of the milk, but here, too, circumstances are such as to make one question the scientific value of these findings, because, while the first examination was made in the intermenstrual period at the end of the seventh month of lactation, the comparative examination made during menstruation was in the thirteenth month of lactation, a comparison which would hardly seem, in the light of our present knowledge, to form a basis for strict scientific deductions.

More recent writers, among them Pfeiffer,³ Schlichter,⁴ and Bamberg,⁵ have been unable to note any changes in the chemical composition of the breast milk during the menstrual period which were greater than individual variations which might occur at any time during the

* Received for publication Feb. 3, 1915.

1. Vernois and Becquerel: *Ann. d'hyg. pub. et de méd. légale*, 1853 (Series 1), lxi, 257 and L, 43.

2. Davis, N. S.: *Northwestern Med. and Surg. Jour.*, 1856, v, 535.

3. Pfeiffer: *Jahrb. f. Kinderh.*, 1883, xx, 359 (392).

4. Schlichter: *Wien. klin. Wchnschr.*, 1889, ii, 978, 1004.

5. Bamberg: *Ztschr. f. Kinderh.*, 1913, vi, 430.

course of lactation. Thiemich,⁶ in his review of the subject, upholds these writers.

Our report, however, has nothing to do with the chemical composition of the breast milk, but rather with the influence of menstruation on the quantity of milk secreted. We were not able to find any definite data in the literature on this subject. Schlichter, however, states that the average daily gain in weight of the child during menstruation was 6 gm. higher than before that period.

REPORT OF CASE

As mentioned in a previous paper,⁷ the baby with a harelip and cleft palate was born on Feb. 26, 1913, after a pregnancy of eight months. According to the hospital regulations at that time the baby was put to the breast every four hours during the first day and after that every three hours for the first week. During the first week he lost 18 ounces. In the second week the milk obtained by the baby was supplemented with breast milk obtained from other women in the hospital. For a few days before the mother and baby left the hospital an attempt was made to make the baby gain in weight by feeding him every two hours. He did gain 4 ounces.

After leaving the hospital on the fifteenth day the baby was given six feedings of 2 ounces each of modified certified milk, half and half, with one teaspoonful of dextrimaltose. In three days he had lost 4 ounces. We increased the feedings to 3 ounces and at the same time began to experiment with the breast pump. In about two days we put together a pump such as described in the other paper and were able to feed the baby with one-half breast milk and one-half modified certified. Inside of a week the baby was fed with six feedings of 3 ounces each of breast milk and began to gain in weight. When a month old he weighed 6 pounds and 3 ounces. From that time on he gained very regularly in weight.

We fed him regularly at four hour intervals beginning at 6 a. m. during the first two months, increasing the amount of each feeding to 3½ ounces during the fifth week and 4 ounces during the eighth week. After the second month we fed him five times daily, 6 a. m., 10 a. m., 2 p. m., 6 p. m. and 12 p. m., increasing the feedings to 4½ ounces during the tenth week, 5 ounces during the eleventh week, 5½ ounces during the thirteenth week, 6 ounces during the eighteenth week, 6¼ during the twenty-second week, 6½ at the end of the six months and as much as we could pump after the seventh month. The first two feedings in the morning were the easiest to obtain, and of the other

6. Thiemich: *Monatschr. f. Geburtsh. u. Gynäk.*, 1898, viii, 659.

7. Caldwell, Fred C.: *An Effective Breast Pump*, page 381, this issue.

three feedings, the 6 p. m. feeding was the most difficult to pump and the least in amount.

When the baby was 6 weeks old the mother's menstrual flow returned and after a few months we noticed that in spite of effort we got a smaller amount of milk at the last three of the daily feedings for about one week before the menstrual flow began. Within two days after the menstrual flow began the amount became normal and in a few days was greater than before that period. This occurrence was so regular that we knew that a menstrual period was coming when the daily total amount of milk began to fail.

The only constant effect of the menstrual period on the baby was that he did not gain so much in weight during the ten days preceding the period as he did the ten days following the period. Sometimes he cried a little more than usual or was a little fretful before the period began, and sometimes during the same time he had a few extra bowel movements with a slight greenish color, but these changes were inconstant.

Our records are most complete for the period which occurred in September, 1913, when the baby was about 7 months old. A careful study of this portion of the record will reveal all of the changes which took place. To get a true picture we will begin ten days before the day on which the menstrual flow began and end with the tenth day after the day.

A glance at the weight curve will show that, with the exception of the first three weeks, for the period of nine months the child showed a perfectly normal gain in weight. As shown in the history, the period of the first three weeks was one in which we were endeavoring to find a means of keeping the child on breast milk. After the institution of the breast pump, as shown in the preceding article, the child went along in an altogether normal manner without any nutritional setbacks.

A glance at the curve showing the quantity of breast milk secreted during four successive menstrual periods is interesting for the following reasons: First, in each instance the occurrence of menstruation marked the beginning of an increased amount of breast milk. In the last three periods this increase was steady and reached its highest point on the thirteenth, eleventh and sixth day, respectively, following the beginning of menstruation. Not only is this true, but it is also true that for several days previous to the occurrence of menstruation there was a distinct reduction in the quantity of breast milk. The first period does not show at what day this reached its lowest point, but in the succeeding three periods we find that the smallest amount of breast milk was secreted respectively on the seventh, sixth and fourth day preceding menstruation and that in the last period there had been a drop

which reached its lowest point on the seventh day previous, showing a distinct tendency in this case toward a decrease in the breast milk, which decrease reached its lowest point about a week previous to the occurrence of the menstrual flow.

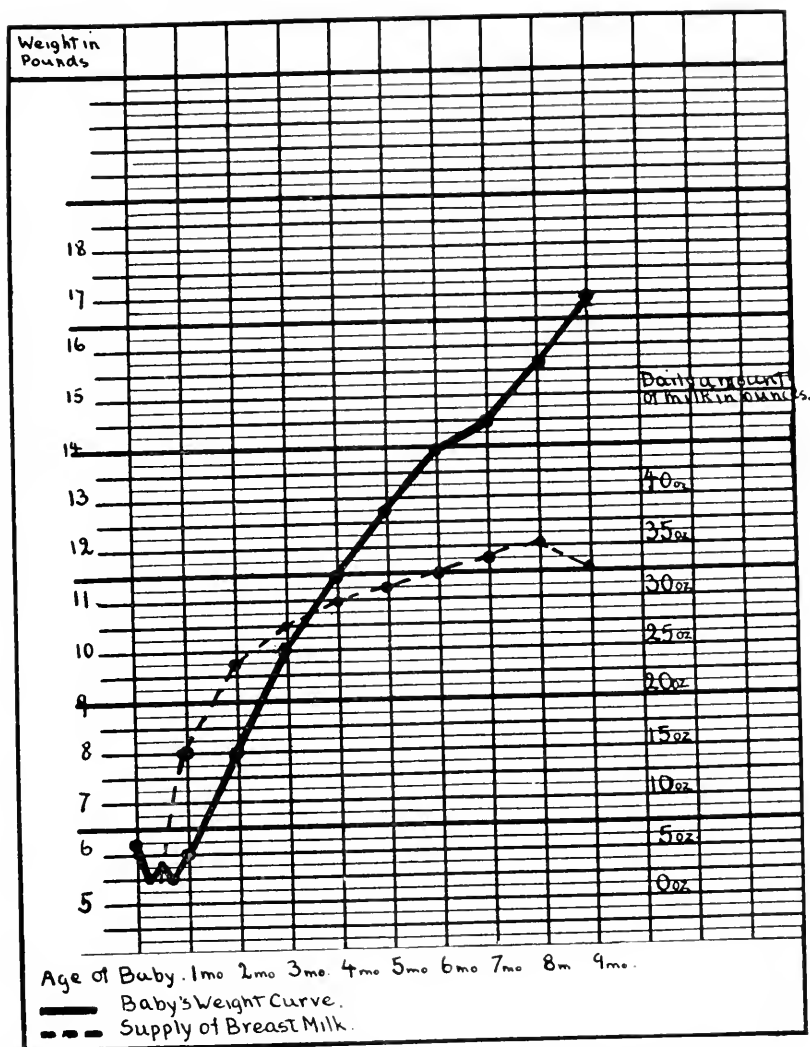


Fig. 1.—Weight curve and amount of breast milk secreted.

The most characteristic months would seem to be the seventh and eighth. In the sixth month the change in the time of the feedings brought about a disturbance in the curve which can readily be seen and which, of course, is not to be reckoned with in this procedure. It is also evident that after the operation, which occurred on November 31,

the regulation in the quantity of breast milk was not the same as it had been previous to that time, and as the first weight curve shows, the total average daily quantity of milk secreted during the ninth month fell below that of the previous two months showing that the breast was probably beginning to give out.

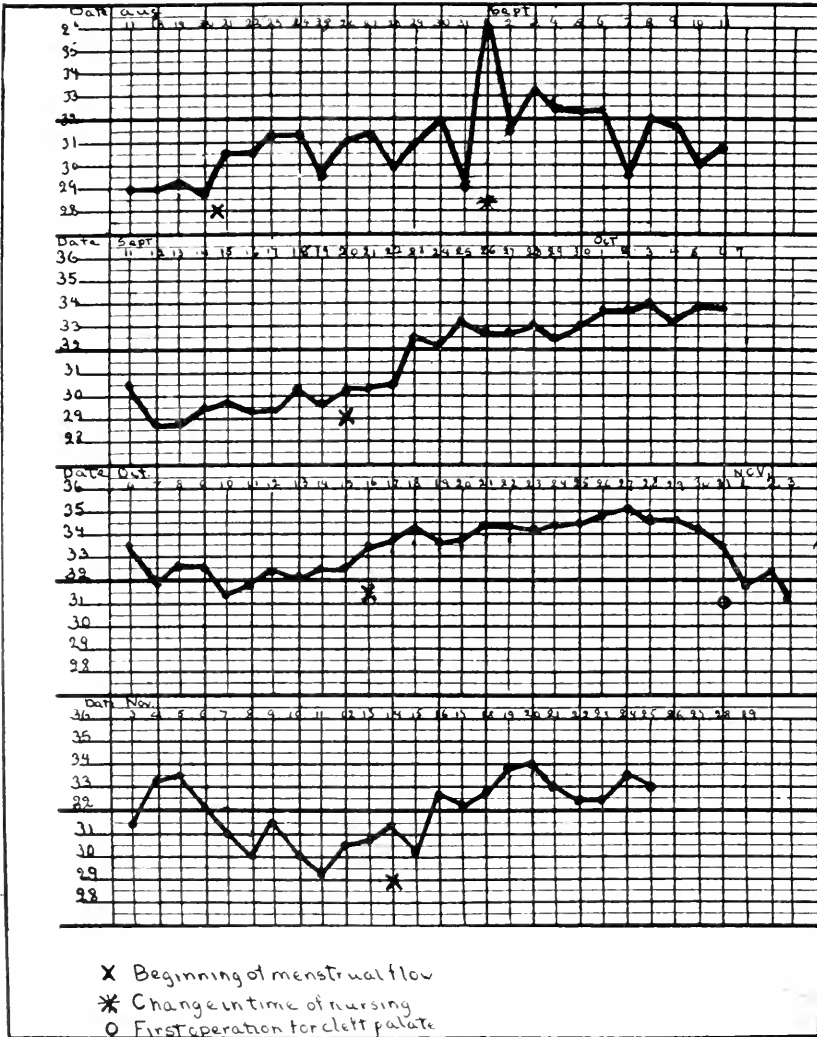


Fig. 2.—Effect of menstruation on the amount of breast milk secreted.

One may say in criticism of the method employed that natural conditions were not present and that therefore these data are of little or no significance. While one cannot deny, of course, that the conditions might have been different had the child been put to the breast, at the

same time there are several things which lead us to think that the method employed does not give us circumstances materially different from those which surround the normal nursing infant. In the first place, while the act of nursing in the young infant certainly shows little or no suction, in the infant which has reached the age of 5 or 6 months there can be no question that the sucking influence is a great, if not the greatest, factor in the withdrawal of the milk from the breast. With the breast pump employed, this suction is exerted in a manner not unlike that used by the infant. In the second place, by using this pump on the wet nurse we have been able to keep up the flow of milk for several months without any apparent tendency to decrease other than might be encountered under normal conditions and have procured in all instances a very satisfactory quantity.

The second objection that may be entered is that the psychic influence would affect the mother in such a way that her efforts to withdraw the milk would be reduced. While the psychic influence is unquestionably of great importance in the flow of breast milk, it seems to us that it would not act under these circumstances in a manner any different from normal. In fact, the period when one would expect the psychic influence to be most marked is that period just previous to and at the beginning of menstruation. In all instances at this time there was a distinct tendency toward an increase in the amount of milk. Since we know so little about the true character of menstruation and the various changes in the physiology of the body which produce it, it seems at this time quite impossible to account for any such variation as is here mentioned.

One other question presents itself and that is that the occurrence of an increased number of stools and a slight tendency to dyspepsia of the breast fed infant during the menstruation period has been too often repeated to be passed by slightly. The only explanation which we could offer for any such occurrence is that during the premenstrual period the quantity of milk is such as to cover amply the needs of the child; in other words, that the maximum amount (von Pirquet) of food is being consumed, and that during and immediately after the menstrual period the increase in the quantity of milk produces a slight degree of dyspepsia.

SUMMARY

We have to do here with a baby born with a harelip and cleft palate, nursed for nine months by means of a specially devised breast pump. The mother's menstrual period began six weeks after birth and continued throughout the nursing. The quantity of milk was carefully measured, especially during the last four months of lactation, and there was shown a distinct relation between the quantity of breast milk and

the occurrence of the menstrual period. This consisted in a period of increase of breast milk beginning with the first day of menstruation and lasting from ten days to two weeks thereafter. There then occurred a diminution in the quantity which reached its lowest point four to seven days previous to menstruation after which there was a gradual increase.

122 South Michigan Avenue—35 South Dearborn Street.

AN EFFECTIVE BREAST PUMP*

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On Feb. 26, 1913, an eight-month baby, with a harelip and cleft palate, was born in the Presbyterian Hospital. Because of the defects in the mouth and his general weakness, the baby was unable to nurse from the breast. He was able to get some milk through a nipple shield if the mother massaged the breast at the same time, but he made such feeble suction that in two weeks the supply of milk amounted to only 2 ounces a day. In the first week the baby lost 18½ ounces, and during the second week, when we supplemented the mother's supply by securing milk from other women who had an overabundance, the baby gained 5 ounces. After leaving the hospital on the fifteenth day, we tried to supplement the breast feedings with certified cow's milk and the baby lost more than he had gained during the second week. I concluded that only breast milk could keep the baby alive.

In desperation I had the father use a nipple shield to stimulate the breasts whenever he was at home, and tried all of the breast pumps I could find. When I could not secure a pump that would enable us to get more than 1 or 2 ounces a day, I tried to make one. After a few days of experimenting, I put together the pump shown in the diagram (Fig. 1).

By using this pump the supply of breast milk was increased so that within a week the baby received 18 ounces a day. The pump was used continuously until December 1 without any other means for stimulation of the breasts. During this time the baby gained 12½ pounds. The increase in the amount of breast milk was gradual but steady, and at no time did we have to give a supplementary feeding. At the end of the eighth month the supply was its highest (35 ounces). The baby had nothing but breast milk and, of course, water.

The chart (Fig. 2) and table show the increase in milk supply and the baby's gain in weight.

MATERIALS NECESSARY

1. A glass T tube made of tubing three-eighths inch in diameter.
2. An ordinary glass nipple shield. One of the shape shown has given the best satisfaction in that there is less obstruction to the flow of the milk.

* Received for publication Feb. 3, 1915.

3. Medium heavy glass tubing three-eighths inch in diameter for the suction tips such as shown in the diagram. These can be easily made by any one who has had a little experience in a chemical laboratory. Two of them can be made from a 10-inch piece of tubing. Heat as narrow a ring as possible in the center of the tube until the glass just softens. Pull very gently until there is a slight constriction in the tube. Then after allowing the glass to cool partially, heat the tube again about one

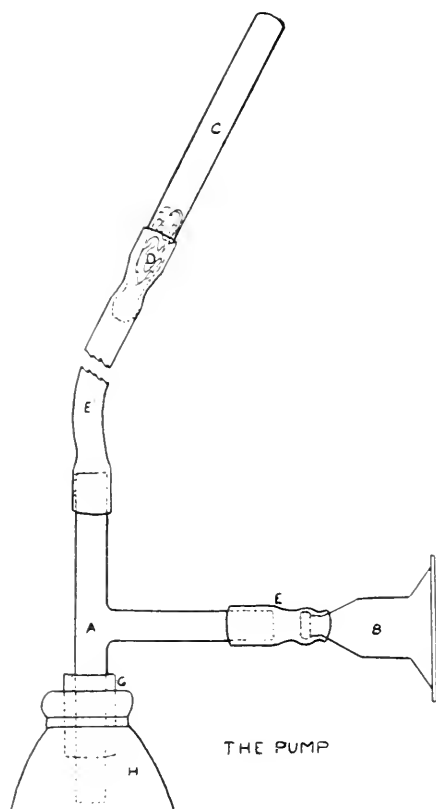


FIG. 1.—Diagram of pump. *A*, T Tube, $\frac{3}{8}$ inch tubing; *B*, glass nipple shield; *C*, suction tip; *D*, cotton plug of sterile absorbent cotton; *E* and *E'*, rubber tubing connections; *G*, stopper of rubber tubing; *H*, nursing bottle.

quarter of an inch beyond the edge of the constriction and make a similar constriction. Repeat the process on the other side of the first constriction. Allow the glass to cool and then file on both sides of the central constriction and break the glass at the file marks, leaving a little of the slanting portion so that the end may be easily pushed into the rubber tubing. Round all of the ends by heating them to redness in

the flame. The constrictions thus made serve to hold the cotton in place and to hold the suction tip firmly in the rubber tubing.

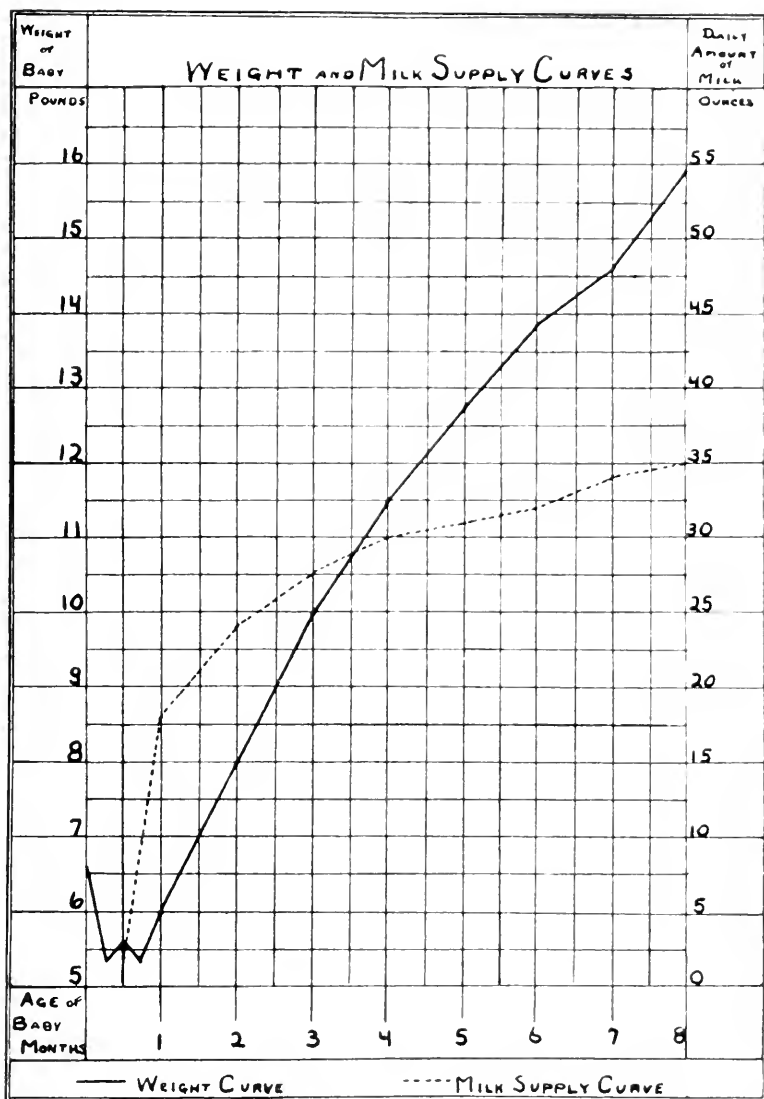


Fig. 2.—Curves of weight of baby and supply of milk, showing increase with use of pump.

4. Non-collapsible rubber tubing of a size that will go over the three-eighths inch tubing and yet will be small enough to make a tight joint with the nipple shield.

5. If the pump is to be used for a considerable time it will be well to have a supply of all parts on hand.

THE ASSEMBLING OF THE PUMP

Though the pump is very simple in construction mistakes can be easily made in putting it together if one is not careful.

1. Join the nipple shield to the side arm of the T tube with a $1\frac{1}{4}$ inch piece of rubber tubing. (A piece just long enough to join them conveniently.)

2. Fit a $7\frac{1}{2}$ inch piece of tubing over one end of the straight part of the T tube and then put a suction tip into the other end of the rubber tubing.

INCREASE IN MILK SUPPLY AND BABY'S GAIN IN WEIGHT WITH USE OF BREAST PUMP

| Date | Weight of Baby | | Daily Amount of Milk | |
|----------------|----------------|--------|----------------------|-----------|
| | Pounds | Ounces | Ounces | Grams |
| February 26... | 6 | 9.5 | Apparently | plentiful |
| March 5 | 5 | 7 | Less | plentiful |
| March 12 | 5 | 11 | 10 | 300 |
| March 19*.... | 5 | 7 | 2 | 60 |
| March 26†.... | 6 | .. | 18 | 240 |
| April 26..... | 8 | .. | 24 | 720 |
| May 26..... | 10 | .. | 27.5 | 825 |
| June 26 | 11 | 8 | 30 | 900 |
| July 26 | 12 | 12 | 31 | 930 |
| August 26.... | 13 | 14 | 32 | 960 |
| September 26.. | 14 | 10 | 34 | 1,020 |
| October 26.... | 15 | 13 | 35 | 1,050 |

* Before using pump. † Pump in use.

3. Make a stopper to fit over the free end of the T tube which will fit the mouth of the nursing bottle. This can be done by pushing a piece of rubber tubing (about $1\frac{1}{2}$ inches) over the end of the T tube and then folding the lower end of the rubber tubing over the upper. It may be necessary to slip a second piece of rubber tubing over the first. The nursing bottles and also the T tubes vary in size and the size of the stopper must be changed for each new combination.

4. See that all connections are air-tight by placing the nipple shield against the cheek or hand and making suction through the suction tip.

CLEANING THE PUMP

1. Before using the pump take it apart and thoroughly clean all parts with soap and water, using brushes. Rinse with clear water. Put the pump together and boil it for five minutes. At the same time the bottle and nipple can be cleansed and boiled.

2. After boiling remove both bottle and pump from the water and without touching the lower part of the stopper or the end of the T tube push the stoppered end of the T tube firmly into the mouth of the nursing bottle.

3. Put a plug of sterile absorbent cotton into the suction tip to prevent saliva from running down into the tubing.



Fig. 3.—Pump in use.

TECHNIC OF PUMPING

Place the suction tip in the mouth. With one hand hold the bottle so that the nipple shield comfortably fits over the nipple. With the other hand massage the breast toward the nipple. At first the mouth will become very tired from the sucking, but one soon grows accustomed to making the necessary suction.

RESULTS

1. By means of this pump alone the mother for whom it was made, nursed her baby for over nine months.

2. The mother's breasts never showed any ill effects.
3. The supply of milk increased gradually month by month from 2 ounces to 35 ounces a day.
4. The baby gained 12 pounds and 11 ounces during the nine months, though we had nearly lost hope when we began to use this pump.
5. At the present time the pump has been successfully used by wet nurses at the Presbyterian Hospital of Chicago. In one case the supply of breast milk increased from 18 to 70 ounces per day and then dropped to an average of 54 ounces a day at the end of five months when the woman went home. The one who is there now, obtains an average of 60 ounces a day. I feel certain that by means of this pump any nursing mother can keep up the supply of milk if she is willing to try.

ADVANTAGES OF THE PUMP

1. The pump is effective.
2. It is so simple that any person can make one. Any of the parts can be purchased at a drug store or a laboratory supply store.
3. The pump can be easily cleaned and sterilized.
4. The milk is pumped directly into a sterile bottle, and without contamination can be kept on ice until needed.
5. The exact quantity of milk given the baby is known.
6. The use of the pump does not injure the breasts in any way or cause any soreness.

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EXPERIENCES WITH THE HIGH CALORIC DIET IN TYPHOID FEVER OF INFANTS AND YOUNG CHILDREN *

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All pediatricists are familiar with the general course, symptoms and complications of typhoid fever in infants and children when the diet has been limited in accordance with the older ideas of the effect of fever on the digestive capacity. In this society studies of typhoid have been recently reported by Drs. Hand and Gittings, by Drs. Koplik and Heiman and by Dr. Griffith.

One of the main features of typhoid fever has always been the marked emaciation, and closely related to the great loss in weight were the lowered resistance to complications and to relapses and the tendency to toxemic nervous symptoms.

The loss of weight in typhoid, as in starvation and in other fevers obeys the general law that the carbohydrate glycogen stored in the body is at first utilized, and after this the fat and the protein. A characteristic feature of the metabolism of prolonged high fever is the marked loss of body nitrogen.

The loss of weight in typhoid has been attributed to (1) partial starvation, (2) the febrile temperature, and (3) the toxic destruction of protein.

Partial starvation has always been recognized, and the effort has been made by most clinicians to prevent the loss in weight by increasing the diet.

Febrile temperature or artificial heat increases protein metabolism, and probably also the metabolism of fat and carbohydrate. To have such an effect the fever must be high and prolonged. The infectious fevers cause a greater loss of nitrogen than starvation or artificial temperatures, so that it has been assumed that the bacterial toxins exert a destructive influence on the body cells. It has been proved by Coleman and his co-workers that in adults it is possible by the high

* Read at the Annual Meeting of the American Pediatric Society, Stockbridge, Mass., May, 1914.

* From the Pediatric Service, First Medical Division, Bellevue Hospital, New York.

caloric diet in typhoid to prevent not only the loss of nitrogen, but the loss of weight as well. Weight equilibrium can be maintained in typhoid patients by a sufficient diet.

The main objections to such a diet are: (1) the patients cannot digest and absorb so much food; (2) the amount of fat will cause alimentary disturbance and acidosis; (3) granted absorption, patients do not require the amount of food advocated.

Du Bois has shown that the typhoid patient has a remarkable capacity to absorb large amounts of food. He concludes from his metabolism studies that typhoid patients, throughout the disease, can absorb carbohydrate and protein as well as normal individuals; they can absorb also very large amounts of fat; but the percentage of

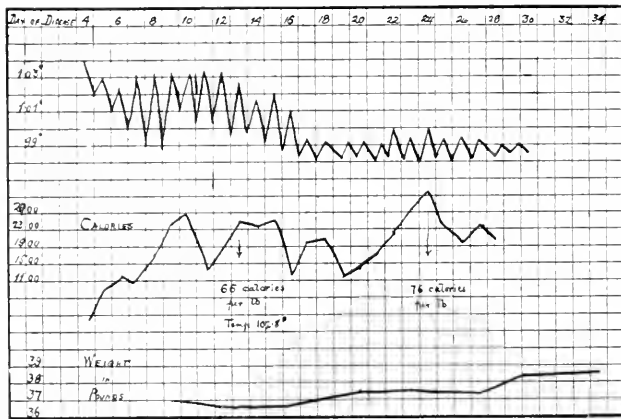


Fig. 1.—High caloric diet in febrile period.

absorption is somewhat lower than the normal, especially in the early part of the disease.

Coleman states that in his 111 cases the increased amount of fat seldom caused any diarrhea, and there was no clinical evidence of acidosis; moreover, no acetone bodies appeared in the urine and the ammonia nitrogen in the urine never exceeded 2 gm., being usually below 1 gm.

As to the food required, it was found clinically that patients lost weight when an excess of food was not given; although an excess of from 1,000 to 2,000 calories were furnished over what the patient expended, there was a loss both of weight and of nitrogen unless such excess was given. In the later stages of the disease the excess is utilized for storing fat.

From the bacteriologic point of view Kendall's¹ studies are important in this connection. He says:

Physiologists have long known that carbohydrate spares body nitrogen, therefore physiological loss of weight due to simple starvation should be largely prevented by such foods. In Coleman's cases not only was the loss of weight attributable to partial starvation prevented, but in addition, practically all the loss attributable to the febrile reaction and to toxemia was markedly reduced. The general symptoms of toxemia were greatly modified.

Kendall further says:

The explanation that presents itself to account for this reduction in toxemia when the patient is on a liberal diet containing an excess of carbohydrates is a simple one. The maintenance of a high physiological sugar content in the body, and consequently in the blood, influences the metabolism of the typhoid

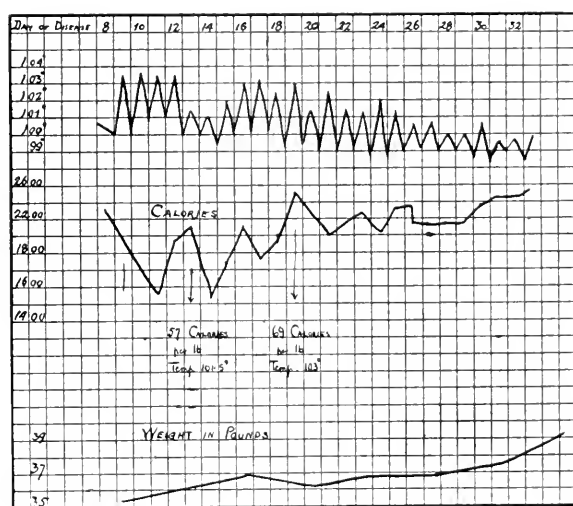


Fig. 2.—High caloric diet in febrile period.

bacilli, directly limiting their action on the body tissues. The typhoid bacilli get their *fuel energy* largely from sugar (dextrose), although their nitrogen requirements are necessarily of protein origin. The waste from the utilization of carbohydrate may be irritative, but is practically never toxic. It is almost certain that the waste products of their *structural* requirements are of comparatively little magnitude. The bacterial waste from fuel needs, particularly when this fuel waste is derived from protein break-down (body tissue in this case) is the more dangerous factor.

It is comparatively simple to understand the changes in the metabolism of the bacteria in the intestinal tract where they are directly in the path of the carbohydrate that is added to the diet and in this connection, the change in the nature of metabolism of the normal endogenous intestinal flora may well play a part. *Bacillus coli*, for example, forms lactic acid in place of indol, if sugars are available. This may lighten the load on the liver and kidneys, since practically no indol is formed to be excreted through the urinary tract. In the body

1. Kendall, Arthur I.: Boston Med. and Surg. Jour., June 5, 1913, p. 825.

itself, on the contrary, the typhoid bacilli might at first sight, seem to be widely separated from utilizable carbohydrate. Automatically, typhoid bacilli cause focal necrosis in the various organs of the body, but it should be remembered that necrotic tissue is readily permeable to crystalloids. It is very probable that the dextrose of the blood, which is maintained at its highest physiological level on a diet rich in carbohydrate (carbohydrate absorption is only slightly impaired in typhoid) seeps into the areas where the organisms are active and therefore reaches them without difficulty. This dextrose is utilized by the typhoid bacilli in preference to the tissue of their host for their fuel. The character of the products of fuel wastes consequently becomes *acid* in place of being alkaline, nitrogenous and toxic, as would be the case of the dextrose content of the blood were diminished. This explanation involves no theoretical difficulties, and the observed clinical results of a liberal carbohydrate diet in reducing the loss of body protein (loss of weight) in suppressing the toxic state, and in general favorably influencing the course of the disease are in accord with the chemical and clinical results observed empirically in many

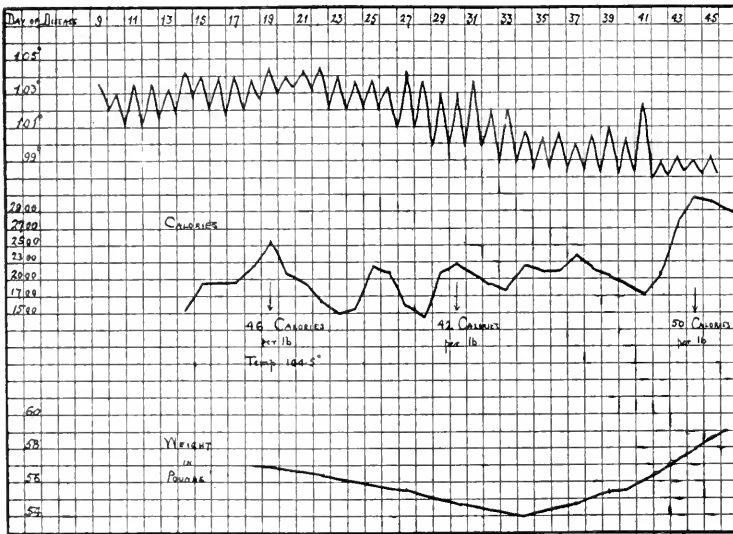


Fig. 3.—High caloric diet in febrile period.

cases where this diet has been introduced. . . . A mortality of 12 among 174 cases of typhoid treated along these lines by Coleman, Croker and Gardner shows what can be done.

Small feedings frequently repeated are important in treating typhoid fever from the bacteriological point of view, so as to maintain a maximal concentration of utilizable sugar, in the intestinal tract and in the body as well. Infrequent feedings fail to do this because the carbohydrate is as a rule rapidly absorbed from the intestinal tract, leaving a residue of protein if the bowel movements are not frequent. The abstraction of the carbohydrate forces the bacteria to utilize protein, be it body tissue or intestinal residuum.

The object of a diet rich in carbohydrate is two fold: *Physiologically* to provide the patient with a readily assimilable food requiring a minimal amount of digestive energy to prepare it for the tissue needs; and *bacteriologically* to shift bacterial metabolism from the destruction of body tissue for their food requirements to the utilization of carbohydrate for at least the major part of their dietary needs. This does not result in annihilation of the invading bacteria, but it certainly approaches their metabolic reformation.

From the point of view of the clinical pathologist, Dr. J. C. Torrey² in a recent communication to the New York Academy of Medicine, stated that the high carbohydrate diet encourages the growth of the acidophils; that on a protein diet, such as milk, the putrefactive type predominated; both he and Dr. Charles Norris, the pathologist of Bellevue Hospital, showed that when acidophil bacteria were present in abundance, it was extremely difficult to recover typhoid bacilli from the stools. High fat diet temporarily restrained the growth of acidophils; but when the carbohydrate was resumed, the acidophils grew rapidly again.

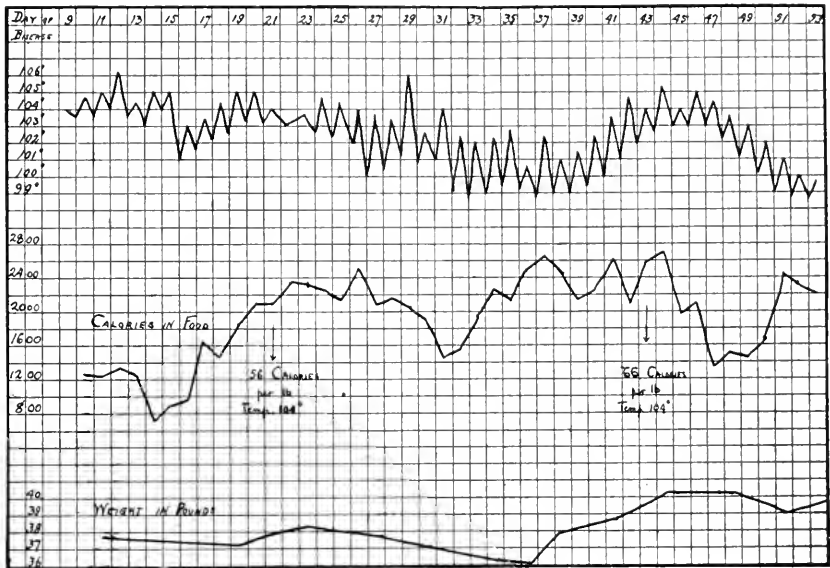


Fig. 4.—High caloric diet. Case with recrudescence.

The metabolism studies of Coleman and Schaeffer and of Du Bois, and the clinical observations of Coleman and his coworkers at Bellevue Hospital, have shown that in adults a much more liberal diet than formerly used is advisable. It was because of interest aroused by this work that we have been anxious to test the value of the high caloric feeding in the typhoid fever of children.

It is seldom that one has the opportunity in New York to see more than an occasional sporadic case of typhoid in children, so that when a considerable epidemic of typhoid occurred in one part of New York, the opportunity was afforded to make a thorough trial of Dr. Coleman's

2. Dr. Torrey's studies have been published under the title, "The Fecal Flora of Typhoid Fever, and Its Reaction to Various Diets," in *The Journal of Infectious Diseases*, 1915, xvi, 72.

plan of feeding. Some results of our experiences with this diet seem worthy of record. For aid and counsel and for valuable suggestions throughout the epidemic, as well as permission to make free quotations from his writings, we wish to thank Dr. Coleman most heartily.

TREATMENT

The routine treatment was sponge baths for temperature of 103.5 F. The patients were kept on the balconies or in rooms with open windows.

Incidentally it may be stated that typhoid vaccine was administered in seven cases, from one to six doses being used, starting with 50 million and increasing by 50 million each successive dose. There was no perceptible influence on the course of the disease.

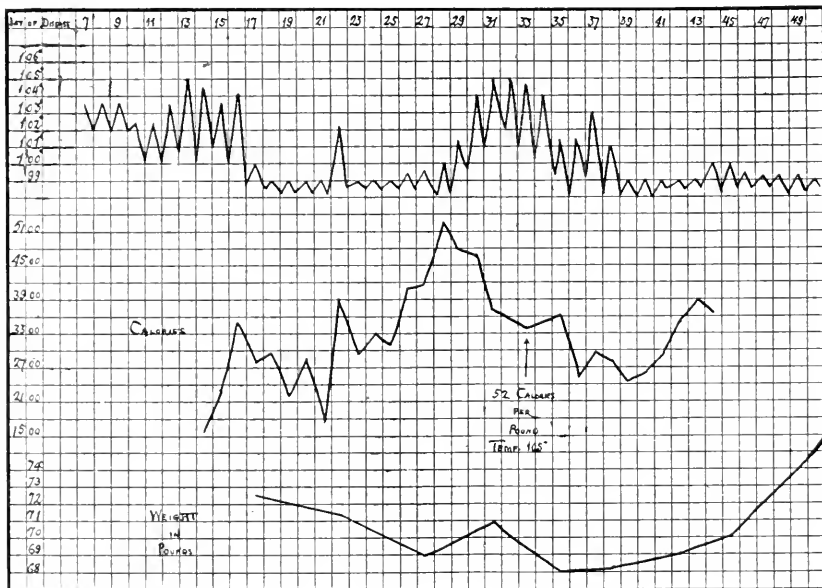


Fig. 5.—High caloric diet in typhoid. Case with relapse.

GENERAL DIET

The children were fed at three-hour intervals, beginning at 6 a. m. and continuing until 9 p. m., six feedings in the twenty-four hours. The articles given were such as would be prescribed for a child in health, with the exception that the only meat used was creamed chicken. In order to increase the caloric value of the liquid food, which was practically always milk, lactose and cocoa and usually cream were added. In no case was an exclusive milk diet used; every patient took cereals in some form. Eggs and toast were offered from the beginning, and it is largely a matter of the nurse's tact and encouragement how

soon a diet high in calories will be taken. At first only a part of the food offered will be taken, and the patient's likes and dislikes must be respected and taken advantage of.

Aside from giving a total amount of food with sufficient caloric value, there must be a certain minimum of protein in the diet. Voit's standard for adults was something over 100 gm. per day, but more recent work has shown that even less would do, but that some 70 gm. should be afforded. Inasmuch as no metabolic studies on children suffering from typhoid have been made, we know of no standard for the daily protein ration in childhood. In our series of cases no attempt was made to have either an upper or a lower limit of protein, but the

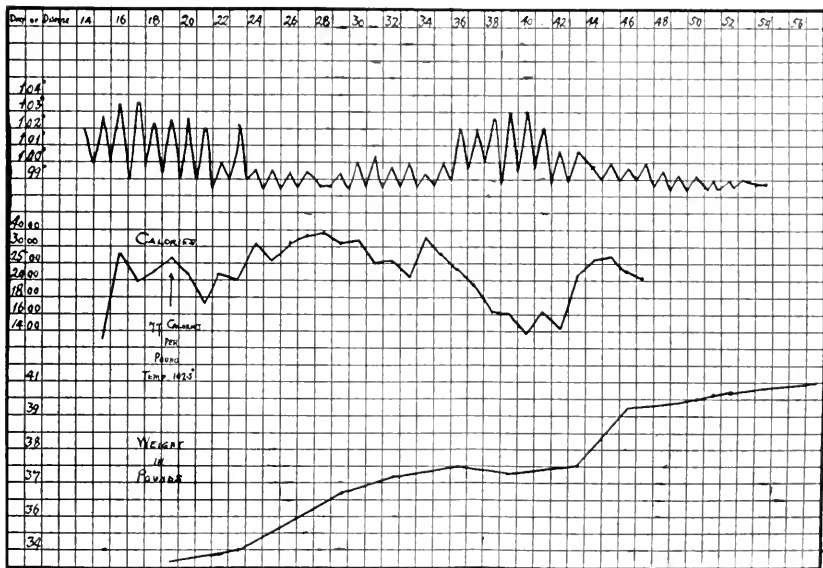


Fig. 6.—High caloric diet in typhoid. Case with relapse.

general rule was adhered to, to have the protein calories not less than 7 nor more than 15 per cent. of the total number of calories given.

Some typical meals of children on the high caloric diet with quantity of food taken and number of calories furnished are given herewith.

TYPICAL DIETS

Angelo R., on the forty-ninth day of disease received 2,214 calories:

6 a. m.: 4 ounces milk, 2 ounces cream, 2 eggs, 2 slices bread.

9 a. m.: 5 ounces milk, 2 ounces cream, 3 crackers.

12 m.: 3 ounces potatoes, 1 egg, 1 slice bread, 6 ounces milk, 2 ounces cream, 2 drams milk sugar.

3 p. m.: 1 ounce ice cream.

6 p. m.: 1 ounce apple sauce, 4 ounces milk, 2 ounces cream, 1 slice bread.

9 p. m.: 4 ounces milk, 2 ounces cream, 2 drams milk sugar.

Leonard B., on November 9 received 2,410 calories:

3 and 6 a. m.: 2 egg-nogs with eggs, $\frac{1}{2}$ ounce milk sugar, 2 ounces cream, 4 ounces milk.

6 a. m.: 4 ounces milk.

9 a. m.: 4 ounces milk, 2 ounces cream, $\frac{1}{2}$ ounce milk sugar, 1 egg (egg-nog), $\frac{1}{2}$ cracker.

12 m.: Egg-nog, 4 ounces milk, 2 ounces cream, $\frac{1}{2}$ ounce milk sugar, 1 egg.

3 p. m.: 4 ounces milk, 2 ounces cream, $\frac{1}{2}$ ounce milk sugar, 1 egg.

6 p. m.: Cocoa, 490 c.c.

9 p. m.: Egg-nog with 4 ounces milk, 2 ounces cream, 2 eggs, $\frac{1}{2}$ ounce milk sugar.

Leonard B., on December 10, during convalescence, received 7,206 calories:

6 a. m.: 10 ounces cereal, 2 eggs, 4 ounces milk, 2 ounces cream, 4 slices bread.

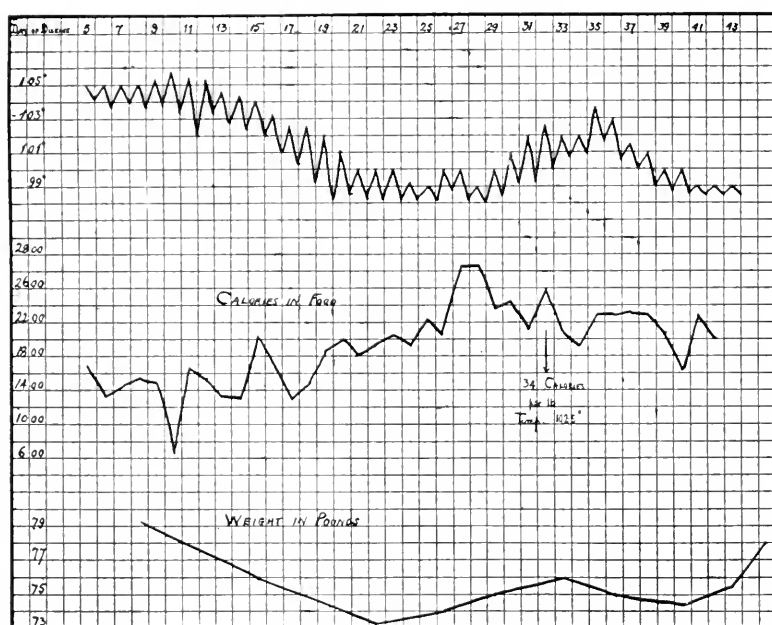


Fig. 7.—High caloric diet. Case with short relapse.

9 a. m.: 4 ounces milk, 2 ounces cream, $\frac{1}{2}$ ounce milk sugar, 4 crackers.

12 m.: 19 ounces potatoes, 6 ounces cream, 4 ounces custard, 8 slices bread.

3 p. m.: 6 ounces milk, 2 ounces cream, 3 crackers.

6 p. m.: 1 egg, 2 ounces apple sauce, 4 slices bread, 4 ounces milk, 2 ounces cream.

9 p. m.: 4 ounces milk, 2 ounces cream, 3 crackers.

J. Corcoran, on the ninth day of disease with temperature ranging from 100 to 103 F., received 2,430 calories:

6 a. m.: 4 ounces milk, 2 ounces cream, $\frac{1}{2}$ slice bread, 1 egg.

9 a. m.: Cocoa, 490 c.c.

12 m.: 4 ounces milk, 2 ounces cream, 1 ounce milk sugar, 1 egg, 1 slice bread.

3 p. m.: 4 ounces milk, 2 ounces cream.

6 p. m.: 4 ounces milk, 2 ounces cream, 1 ounce milk sugar, 1 egg, 1 slice bread.

9 p. m.: 4 ounces milk, 2 ounces cream.

The calculations of the caloric values were made from the following list prepared by Dr. Coleman:

FOOD VALUES — SOLIDS

| Food | Amount | Calories |
|----------------------|---|----------|
| Apple sauce | 1 ounce | 30 |
| Bread | Average slice (33 gm.) | 80 |
| Butter | 1 pat ($\frac{1}{3}$ ounce) | 80 |
| Cereal | 1 heaping tablespoonful ($1\frac{1}{2}$ oz.) | 50 |
| Crackers | 1 ounce | 114 |
| Cream (20 per cent.) | 1 ounce | 60 |
| Custard | 4 ounces | 250 |
| Cream chicken | 1 ounce | 50 |
| Egg | 1 (2 ounces) | 80 |
| Egg (white) | 1 | 30 |
| Egg (yolk) | 1 | 50 |
| Lactose | 1 tablespoonful (9 gm.) | 36 |
| Milk (whole) | (1 pint 350 gm.) 1 ounce | 20 |
| Potato (whole) | 1 medium | 90 |
| Potato (mashed) | 1 tablespoonful | 70 |
| Rice (boiled) | 1 tablespoonful | 60 |
| Sugar, cane | 1 lump | 16 |
| Sugar, milk | 1 tablespoonful (9 gm.) | 36 |
| Toast | Average slice | 80 |

For practical purposes, the milk sugar may be measured in a medicine glass.

Each measured ounce equals 18 gm. in weight. If milk sugar is added to water in the proportion of 24 gm. to 30 c.c., and the water brought to the boiling point, the milk sugar is completely dissolved. Such a solution made daily, or just before use, will be found convenient in administering the diet.

FOOD VALUES — LIQUIDS

| | |
|---------------------------------|-----------|
| Cocoa with milk: | Calories |
| 1 rounding teaspoonful of cocoa | 50 |
| 2 ounces of milk sugar | 240 |
| 4 ounces of milk | 80 |
| 2 ounces of cream | 120 |
| | <hr/> 490 |

Mix the sugar and cocoa; cook in the milk until dissolved. Serve with cream.

| | |
|--------------------------------|-----------|
| Cocoa with cream: | Calories |
| 1 heaping teaspoonful of cocoa | 50 |
| 2 ounces of milk sugar | 240 |
| $\frac{1}{2}$ cup of water | ... |
| 3 ounces of cream | 180 |
| | <hr/> 470 |

Mix the cocoa and sugar, add the water and boil. Then add the cream, or use less cream and serve with whipped cream.

| | |
|----------------------------------|-----------|
| Coffee: | Calories |
| 1½ ounces of milk sugar..... | 180 |
| 4-5 ounces of strong coffee..... | 120 |
| 2 ounces of cream | 120 |
| | <hr/> 300 |

| | |
|--|----------|
| Lemonade: | Calories |
| 4 ounces of milk sugar | 480 |
| 7 ounces of cold water | ... |
| 2 tablespoonfuls of lemon juice (or to taste)..... | ... |

Boil the sugar and water for two minutes, add lemon juice to taste, strain and cool.

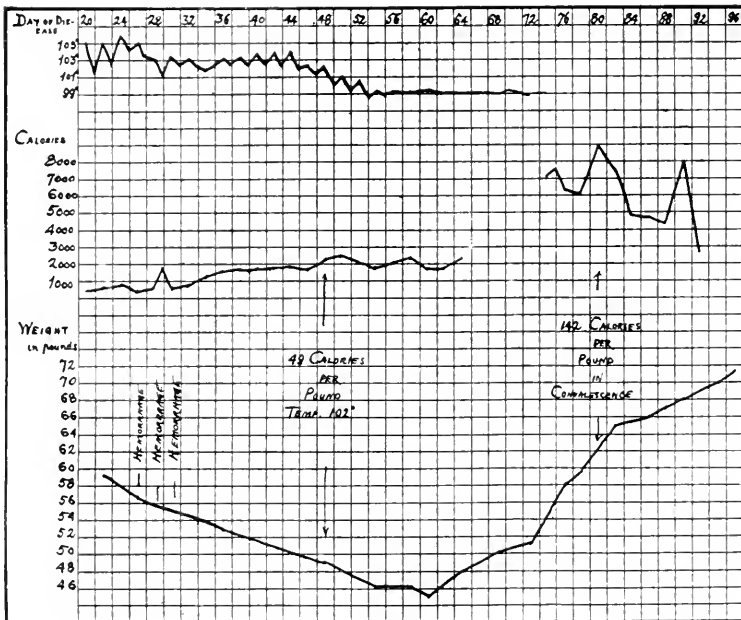


Fig. 8.—Severe case with hemorrhages. Shows loss of weight in spite of liberal feeding during febrile period, but rapid gain in convalescence while taking food of very high caloric value.

The number of calories that were actually taken after the first few days, and that seemed from a clinical point of view to have been satisfactorily utilized, varied from 100 to 300 calories per kilogram. As regards utilization of the food the urine in these cases very seldom showed any more than a slight trace of indican.

It was at first thought that a high range of temperature would in itself interfere with the taking of so much food; this was found to be partially true, but unless toxic nervous symptoms were present, the fever did not prevent the child from taking a generous diet; as the temperature fell, however, the amount of food taken was greater.

The diagnosis was established by positive Widal reaction in forty-four cases and by positive blood cultures in thirty-six cases. In only

one case was there found neither a positive Widal nor a positive blood culture. A complete history of each patient in this series will be found in Tables 1, 2 and 3.

The age range of the patients was as follows: Under 2 years 1 case; from 2 to 6 years, 21 cases; from 7 to 12 years, 26 cases, making a total of 48 cases.

COURSE OF THE DISEASE

The length of time in the hospital averaged twenty-eight days; extremes from thirteen to seventy-nine days. Hand and Gittings report that the average stay in the hospital in their 145 cases was thirty-one days. The ages in their cases ranged from infancy to 12 years, the greater number of the patients being from 4 to 9 years. The day of the disease, as nearly as could be estimated, on which the temperature became normal was found on the average to be the twenty-eighth. Extremes from fifteen to sixty-eight days.

SYMPTOMATOLOGY

The general condition of the patients was remarkably good. The so-called typhoid state occurred in much smaller proportion than under the old methods of treatment, so that the patients did not present, except in rare instances, the typical appearance of typhoid fever.

Abdominal distention.—This was present in only six cases, and in but one of these was it severe or troublesome.

Hemorrhages.—Five patients had, at some time during the course of the disease, blood in the stools. In only two cases were the hemorrhages severe enough to cause any apprehension. In both, blood transfusion was done by the Lindemann method, a procedure which was developed in our wards, and each time with signal benefit. One of the patients, Leonard B., already referred to, was transfused three different times, the amount of blood given being 160 c.c. paternal, the first time, 260 c.c. paternal the second time, and 280 c.c. paternal the third time. This was the patient who lost the greatest amount of weight and who, during his convalescence, took the largest number of calories we have ever seen recorded, namely, 8,000 in twenty-four hours or 310 calories per kilogram. The reason this enormous amount of food was permitted was because of the boy's constant clamor for a cracker or any form of food to satisfy his gnawing hunger. The eternal call for another cracker induced us to let him eat his fill for a few days, with the result reported. He gained in weight from 45 to 72 pounds in thirty-seven days, an average gain per day of about $\frac{3}{4}$ of a pound.

Nervous Symptoms.—Thirteen patients were irrational in the early stage of the disease. One who came in during the latter part of the second week of his illness presented the picture of a severe psychosis, a type of nervous disturbance occasionally seen late in the course or

TABLE I. GENERAL HISTORY OF PATIENTS IN CASES I to 43

| Case No. | Name | Age, Years | Prodromal Period, Days | Time in Hospital, Days | Chief Complaint | Nose Bleed | Rose Spots | Spleen Enlargement | Bowels |
|----------|-------------------------|------------|------------------------|------------------------|--|------------------------|--------------------|--------------------|------------------------|
| 1 | S. Silverman..... | 1 1/2 | 3 | 32 | Fever | None | ++ | None | Diarrhea, regular |
| 2 | Freda Gerke..... | 2 | 10 | 28 | Fever | None | ++ | None | Loose. |
| 3 | G. Geche..... | 3 1/2 | 7 | 23 | Headache; tire; fever; pain in stomach | None | Appeared in 4 days | + | No diarrhea, costive. |
| 4 | A. Dunn..... | 4 | 2 | 27 | Headache; pain in abdomen | None | ++ | ++ | No diarrhea, costive. |
| 5 | Margaret Kronek..... | 4 | 7 | 14 | Fever; headache | ? | None | None | No diarrhea, costive. |
| 6 | N. Wuchinsky..... | 4 | 7 | 20 | Abdominal pain; headache... | None | ++ | ++ | Costive. |
| 7 | W. Githart..... | 4 1/2 | 13 | 16 | Malaise | Yes | ++ | ++ | Costive. |
| 8 | Sadie Penna..... | 4 1/2 | 14 | 26 | Abdominal pain; fever..... | None | ++ | ++ | Costive. |
| 9 | H. Attmador..... | 5 | 3 1/2 | 4 | Fever | None | ? | None | No diarrhea, costive. |
| 10 | Joseph Cochran..... | 5 | 7 | 28 | General malaise | None | None | ? | No diarrhea, costive. |
| 11 | Catherine Shea..... | 5 | 6 | 19 | Headache; fever | None | ++ | + | Loose. |
| 12 | M. Geche..... | 5 | 5 1/2 | 25 | Headache; fever; pain in stomach | Negative | +++ | + | None. |
| 13 | R. Zingales..... | 5 | 5 | 31 | Malaise; headache; fever..... | None | ++ | None | Slight diarrhea. |
| 14 | Rose Zingales..... | 5 | 4 | 21 | Headache; fever | None | ? | None | Diarrhea. |
| 15 | George Zait..... | 5 | 8 | 22 | "Pain in belly" | None | + | None | Slight diarrhea. |
| 16 | Rocco Garbali..... | 6 | 2 | 18 | Fever; headache | None | None | ++ | Costive. |
| 17 | Aaron Psan..... | 6 | 8 | 16 | Fever; headache | ? | None | None | No diarrhea. |
| 18 | E. Corcoran..... | 6 | 7 | 19 | Pain in right side..... | None | None | ++ | Costive. |
| 19 | Jas. Sloan..... | 6 | 3 1/2 | 43 | Fever; occipital; sudden onset; three days | ? | None | ++ | Costive. |
| 20 | Catherine Dorso..... | 6 1/2 | 4 | 14 | Fever | None | ++ | +++ | Costive. |
| 21 | John Kelleper..... | 7 | 8 | 47 | Fever; sleepiness; pain in stomach | ? | None | ++ | Diarrhea for one day. |
| 22 | Mike Forlenza..... | 7 | 14 | 28 | Headache | None | Few ? | None | Constipated. |
| 23 | Mary Mancun..... | 8 | 9 | 52 | Fever; headache | None | ++ | ++ | Constipated. |
| 24 | Thos. O'Brien..... | 8 | 7 | 15 | Headache; fever | + 5 days after admn. | ? None | None | Constipated. |
| 25 | Coro Gusclau..... | 8 | 5 | 17 | Headache; pain in stomach; | ? | +++ | ++ | ? More open than usual |
| 26 | Olga Medvill..... | 8 | 3 | 23 | Headache; fever | None | ++ | ++ | Costive. |
| 27 | Mary Grossman..... | 8 | 14 | 44 | Headache | None | +++ | ++ | Loose. |
| 28 | Julie Schluppe..... | 8 | 10 | 28 | Headache | Slight | ++ | ++ | Costive. |
| 29 | Josephine Zanger..... | 9 | 30 | 30 | Fever | + | ++ | ? | Constipated. |
| 30 | Josie Crompton..... | 9 | 7 | 27 | Vomiting; headache | ? | None | None | None. |
| 31 | Mary Piazza..... | 9 | 5 | 34 | Fever; headache | None | ++ | ++ | Costive. |
| 32 | Angelo Rone..... | 9 | 10 1/2 | 16 | Fever | None | ? | + | Diarrhea. |
| 33 | Abe Psan..... | 9 | 10 | 23 | Headache; fever | None | ++ | + | Costive. |
| 34 | John Purcell..... | 9 | 10 | 23 | Fever; loss of appetite..... | Negative | +++ | + | Costive. |
| 35 | A. Damprosio..... | 10 | 7 | 13 | Fever; pain in abdomen; headache | None | +++ | + | No diarrhea. |
| 36 | Mary McKenna..... | 10 | 6 | 17 | Fever; anapathic | None | +++ | ++ | Costive. |
| 37 | W. Melville..... | 10 | 7 | 31 | Chilliness; fever | None | ++ | ++ | No diarrhea. |
| 38 | Angelina Garbali..... | 10 | 5 | 22 | Fever; headache | None | ++ | + | Costive. |
| 39 | C. McCarthy..... | 10 1/2 | 7 | 26 | Tire; fever; pain in neck for two days but no headache | Yes | + | + | No diarrhea. |
| 40 | F. Windberg..... | 11 | 6 | 43 | Loss of strength and appetite; fever and slight cough | None | ? | + | Constipated. |
| 41 | Sophie Grlansky..... | 11 | 3 | 44 | Headache | Slight on day of admn. | ++ | None Later ? | Not felt |
| 42 | Rose Newman..... | 11 | 7 | 42 | Headache; general malaise..... | None | ++ | ++ | No diarrhea. |
| 43 | Leonard Bisnigians..... | 11 | 19 1/2 | 79 | Fever | None | ++ | Not felt | |

* There is some question as to the length of convalescence.

† Cough 1 1/2 months. ‡ Confined to bed at once.

§ Sudden onset.

|| Sick before admission.

TABLE 2.—TESTS MADE AND COMPLICATIONS SEEN IN CASES 1 TO 43

| Case No. and Dis- tention | Hemorrhages | Blood Counts | Widal and Blood Culture | Urine | Other Complications |
|---|---|---|---|---|---|
| 1—None | None | 9/7: H, 500 W. C.; P. 42; Ly., 58. 9/10: 17,500 W. C.; P., 57; Ly., 33; L. mono., 6; Traps, 2; Baso., 2. 9/25: 12,500 W. C.; P., 50; Ly., 50. | 9/10: W., paratyphoid, pos. | 9/7: Albumin light cloud. Sugar, 0. | Both great toes and fourth and fifth fingers of left hand have pus. Double outils. Gastro-enteritis. Pus shows B. paratyphoid. |
| 2—None; held tense. | None | 9/25: 12,500 W. C.; P., 50; Ly., 50. | 9/23: W. pos.; 9/27: B. c., pos. | None | No vomiting. |
| 3 None | None | 9/13: 17,000 W. C.; P., 60; Ly., 40. 9/22: 10,000 W. C.; P., 34; Ly., 61. | 9/18: W., pos. 9/20: B. c., pos. | 9/18: W., pos. 9/20: B. c., pos. | Refused part of feeding on first four days. Not afterward. Vomited, 10 17, 19, 21. |
| 4—Slight for two weeks. | None | 9/22: 15,500 W. C.; P., 55; Ly., 45. | 9/18: W., pos. 9/20: B. c., pos. | 9/23: Fl. trace alb. Sugar, 0. Few leu- kocytes. | Slept fairly well during vomiting period. No mental disturbance. |
| 5 None | None | 9/16: 12,200 W. C.; Ly., 76; P., 15; L. mono., 9. | 10/3/13: Widal neg. 9/20: W. pos. 9/22: B. c., pos. | 9/23: Sugar, 0. Albu- min, 0. | None. None. |
| 6 Slight on admis- sion and for ten days; then soft. | Streak of blood on October 3. | 10/14: 9,200 W. C.; P., 43; Ly., 57. | 10/13: W. pos. 10/18: B. c., neg. | None | None. |
| 7—None | None | 9/26: 5,000 W. C.; P., 58; Ly., 42. | 9/27: W. pos. 10/1: B. c., pos. | None | None. |
| 8 None | None | 10/9: 6,200 W. C.; P., 50; Ly., 50. | 10/9: W., pos. | None | Bronchitis? Mucles By. Roentgen ray military nodules found. |
| 9 None | None | 9/30: 10,000 W. C.; P., 66; Ly., 34. | 10/2: W. pos. 10/4: B. c., neg. | None | Stye on left eye. Otherwise none. |
| 10 None | None | 10/9: 13,400 W. C.; Ly., 20; P., 80. | 9/18: W. pos. 9/20: B. c., neg. | None | Vomited three days. October 3, 4, 6, Vomited twice. Otherwise none. |
| 11 None | Slight trace of blood on December 2. No change of diet. | 9/7: 23,000 W. C.; P., 66; Ly., 34. 9/16: 15,500 W. C.; P., 60; Ly., 59; Baso., 1. | 9/23: W. pos. 9/27: B. c., pos. | 9/20: Albumin, 0. Su- gar, 0. Moderate No. of leukocytes. | None. |
| 12 Slight, on ad- mission in ill- through course. Never rigid. | None | 18,000 W. C.; P., 67; Ly., 33. | 9/23: W. pos. 9/27: B. c., pos. | None | Echymosis over left eye. None. |
| 13 None | None | 1/28: 9,500 W. C.; P., 56; Ly., 44. | 10/29: W., pos. B. c., pos. | 1/11. 1/12. 1/14: Albu- min, neg. Casts, neg. | Readmission; appetite poor until Octo- ber 9. Then very good. |
| 14 None | None | 9/19: 23,400 W. C.; P., 77; Ly., 15; L. mono., 8. 9/23: 11,500 W. C.; P., 63; Ly., 37. | 9/22: W., pos. 9/25: B. c., neg. | Sugar, neg. Ind., neg. 9/24: Albumin, faint trace. Sugar, 0. Casts, 0. | Few crackling rales noted September 20 and September 22 at left apex and right base. Cleared up before discharge. |
| 15 9 19, none; 9/20, slight; 9/25, none. | None | 10/15: 4,000 W. C.; P., 71. Ly., 29. | 10/16: W., pos. 10/18: B. c., pos. | None | No nervous symptoms at any time. |
| 16 None | None | 9/20: 6,600 W. C.; P., 56; Ly., 42; L. mono., 2. | 9/22: W., pos. 9/25: B. c., neg. | Albumin, trace. Sugar, 0. Few hyaline casts. | None. |
| 17 None | None | 10/9: 6,000 W. C.; P., 75; Ly., 25. | 10/10: W., neg. 10/14: B. c., pos. | None | None. |

TABLE 2.—TESTS MADE AND COMPLICATIONS SEEN IN CASES 1 TO 43—(Continued)

| | | | | | | |
|--|---|--|--------------------------------|--------|---|---|
| 33—None | None | 9/20: 9,800 W. C.; P., 49; Ly., 49; L. mono, 2. | 9/22: W., pos. B. c., pos. | 9/25: | Albumin, marked trace. Few hy., 0. Gr. casts. | Ring worm on scalp. eruption. Wassermann positive. Father's Wassermann strongly positive. |
| 34—None on admission; held abdomen tense. Later soft. | None | 9/18: 7,600 W. C.; P., 38; Ly., 53; L. mono, 6; Eo., 3. 9/24: 6,500 W. C.; P., 60; Ly., 40. 9/29: 15,000 W. C.; P., 78; Ly., 22. | 9/22: W., pos. B. c., pos. | 9/25: | 9/23: Albumin, faint trace. Sugar, 0. Ca. oxal crystals. 9/25: Albumin, faint trace. No sugar. No casts. | Delirious, very drowsy for six or seven days. Then brighter gradually. Bronchopneumonia with many small abscesses in right lower lobe. |
| 36—None. Slight tenderness over abdomen on admission. | None | 9/19: 7,400 W. C.; P., 51; Ly., 41; L. mono, 5. | 9/22: W., pos. B. c., pos. | 9/25: | 9/13: Albumin, very faint trace. Sugar, 0. Sediment, 0. | None. |
| 37—Complained of abd. pain, but not distended. Cleared up quickly. | None | 9/13: 9,000 W. C.; P., 71; Ly., 29. 10/14: 7,000 W. C.; P., 25; Ly., 75. | 9/14: W., pos. B. c., pos. | 9/16: | 9/14: Albumin, faint trace. Few leukocytes. Hyaline casts. Amorph. urates. Sugar, 0. | Scoliosis. Otherwise none. |
| 38—None | None | 10/13: 6,600 W. C.; P., 66; Ly., 34. | 10/13: W., pos. B. c., pos. | 10/14: | None | Vomited several time. Uneventful recovery. |
| 39—None | None | 9/10: 5,000 W. C.; P., 71; Ly., 29. | 9/11: W., pos. B. c., neg. | 9/14: | Slight trace of albumin. | None. |
| 40—None during relapse. | None | 9/22: 9,500 W. C.; Ly., 59; P., 41. 9/24: 12,500 W. C.; P., 48; Ly., 42. | 9/3: W., pos. B. c., pos. | 9/6: | 9/3: Albumin light cloud. Sugar, 0. 9/14: Albumin, 0. Sugar, 0. | None. |
| 41—Full but not distended. | None | 10/18: 11,000 W. C.; P., 50; Ly., 50. 10/31: 9,000 W. C.; P., 47; Ly., 53. 11/21: 9,000 W. C.; P., 51; Ly., 49. | 10/18: W., pos. B. c., pos. | 10/20: | 11/11. 11/12. 11/14, 11/26: Albumin, sugar and indican, neg. | Boil on right thigh. Vomited once before admission. |
| 42 9/21, slight; 9/24, abd. soft. Soft thereafter. | None | None | 9/5: W., pos. B. c., neg. | 9/9: | 9/24: Albumin, faint trace. Sugar, 0. | Bronchitis for first three weeks. Nose bleed. |
| 43—Moderate on admission. | 10/17: slight; 10/18: 3; 10/19: severe; 10/20: 2; 2 sev.; 1 slight, 10/21: blood in stool; 10/22: hemorrhage. | 10/13: 19,000 W. C.; P., 51; Ly., 43; L. mono, 5; Baso., 1. 10/19: 6,600 W. C.; P., 60; Ly., 40. 10/22: R. C., 4800,000; Hb., 58%; 10/24: 16,000 W. C.; P., 24; Ly., 76. 10/26: 9,500 W. C.; P., 44; Ly., 56. 10/28: 8,500 W. C.; P., 40; Ly., 60; R. C., 3,500,000; Hb., 45%. 11/13: 10,000 W. C.; P., 41; Ly., 51; Hb., 53%; R. C., 2,500,000. 11/17: 6,200 W. C.; P., 36; Ly., 70; Hb., 50%; R. C., 3,000,000. 12/10: Hb., 79%; R. C., 5,700,000; W. C., 17,000; P., 41; Ly., 59. | 10/18: W., pos. B. c., pos. | 10/20: | Triple phos. 11/26: Albumin, trace. Sugar, 0. Indican? 12/8: Albumin, trace. Sugar, 0. Indican, trace. 12/26: Albumin, neg. Sugar, neg. Indican, neg. 10/22: Albumin, mod. trace. Few hyaline and granular casts. Few leukocytes. | Acute bronchopneumonia. Acute hepatitis? Cholecystitis? De- cubitus. Acute myocarditis. |

TABLE 3. RELATION OF FEEDING TO GENERAL COMFORT AND NERVOUS SYMPTOMS

| Case No. | Relapses | Condition of Patient | Medicines | Vaccine |
|----------|--|--|-------------------------------|---|
| 1 | None..... | Extremely irritable for three weeks. Appetite never good | Hexamethylenamin..... | None. |
| 2 | None..... | Extremely irritable during entire stay, but never really sick. Appetite fair. | None..... | None. |
| 3 | None..... | Very nervous and irritable for ten days during which appetite was poor; then better. Condition continued better, as did appetite. | Hexamethylenamin last 7 days. | None. |
| 4 | None..... | Restless on admission. Mentality not impaired. Apathetic and irritable for first two and one-half weeks. | None..... | None. |
| 5 | None..... | Child was in excellent condition from start to finish. | None..... | 10/30, 200 million. |
| 6 | None..... | Apathetic first few days. Later good. Appetite good..... | Hexamethylenamin..... | None. |
| 7 | None..... | Very irritable and ill on admission. Appetite fairly good. No nervous symptoms. | None..... | None. |
| 8 | None..... | Abdomen held tense on admission. Quite restless for first week. Appetite then good. | None..... | None. |
| 9 | | Had a few rales at bases..... | | None. |
| 10 | None..... | Appetite poor for nine days. General condition always good. No nervous symptoms. | None..... | None. |
| 11 | None..... | Not stuporous or prostrated on admission. Cried a great deal first few days. Appetite poor ten days then good. No nervous symptoms. | None..... | None. |
| 12 | None..... | Appetite poor for five days; then better. No mental disturbance after six days. | Hexamethylenamin..... | None. |
| 13 | None..... | Abdomen held tense. Appetite poor for eighteen days. Very quiet for first two weeks. No nervous symptoms. | None..... | None. |
| 14 | This attack was a relapse | Very quiet but never had nervous symptoms..... | None..... | None. |
| 15 | None..... | Appetite very poor until October 3. Very uncomfortable until September 26, when general condition of nervousness became better. Had headache and was restless. | Calc. Sod. Benz..... | None. |
| 16 | None..... | Appetite poor first few days; good for two days then poor again. Picked up finally and had good appetite. | None..... | None. |
| 17 | None..... | Appetite poor first seven days; then good. Little sleep first two days; then bright. | Hexamethylenamin..... | None. |
| 18 | None..... | Appetite poor but general condition good. Appetite better after four days. No nervous symptoms. | None..... | None. |
| 19 | None..... | | Pod. Cit. Urol. Calc. Laet. | None. |
| 20 | None..... | Always in good condition. Apathetic for a day or two, but then better. | None..... | None. |
| 21 | None..... | Had good appetite from start. Never very sick..... | Hexamethylenamin..... | None. |
| 22 | None..... | Appetite poor for ten days. Very quiet..... | None..... | None. |
| 23 | On fortieth day, but no additional symptoms. | September 14, pulse imperceptible. September 16, rational for first time. September 18, irrational again. September 19, brighter. | None..... | 9/22, 50 million; 9/24, 50 million; 9/26, 100 million; 9/28, 100 million; 9/30, 150 million; 10/2, 200 million. |
| 24 | None..... | Appetite and general condition always good..... | None..... | 200 million. |
| 25 | None..... | Appetite usually poor; no disturbance of mentality. Well at all times. | Hexamethylenamin..... | None. |

| | | | | | |
|----|--|--|---|-------|--|
| 26 | None..... | Apathetic for first few days. Appetite good always..... | Hexamethylenamin..... | None. | |
| 27 | Relapse, but general condition remained excellent..... | Appetite good for first ten days; rather poor on September 15 and 16, but nervous condition at all times good. Up in chair September 20 for two hours till September 26; then to bed again. Appetite good. | Hexamethylenamin..... | None. | |
| 28 | None..... | Appetite poor for first week. Never very sick..... | None..... | None. | |
| 29 | None..... | Hemorrhage day after admission and two days later. Transfused and horse serum 30 c.c. injected. Father's blood used in transfusion. Restless and irrational till October 3. | 9/20, 15 c.c. horse serum; 10/1, 30 c.c. paternal blood; 10/3, 20 c.c. horse serum; Cafe. Lact.; hexamethyl- enamin. None..... | None. | |
| 30 | None..... | Refused food for first week. No nervous upsets except headache. | Hexamethylenamin, salol. | None. | |
| 31 | None..... | Delirious for nineteen days with marked meningeal symptoms. Double ankle clonus; stiff neck. Spinal cord tap cells 3. Noguchi negative. Appetite improved October 7. | Hexamethylenamin..... | None. | |
| 32 | None..... | Child was admitted in delirium with meningismus. November 12. Temperature dropped from 105 to 97.6 F. For ten days was nervous and very restless. | Hexamethylenamin..... | None. | |
| 33 | None..... | Stupid for two days but always had a good appetite..... | Hexamethylenamin last 5 days. | None. | 9/22, 50 million; 9/24, 50 million; 9/26, 100 million; 9/28, 100 million; 9/30, 100 million; 10/1, 100 million; 9/28, 50 million; 9/30, 150 million; 10/2, 200 million. |
| 34 | None..... | Appetite very poor for seven days then gradually improved. Comfortable first on October 2. | Hexamethylenamin..... | None. | 9/11, 50 million; 9/13, 50 million; 9/15, 100 million; 9/17, 100 million; 9/19, 100 million; 9/22, 200 million. |
| 35 | None..... | Irrational from second day onward..... | Hexamethylenamin..... | None. | |
| 36 | None..... | Appetite good from start. No nervous disturbance..... | None..... | None. | |
| 37 | None..... | For first two weeks was very apathetic and irrational the first few nights, then better; appetite poor usually; good the last two weeks. | Hexamethylenamin seven days. | None. | |
| 38 | None..... | Appetite only fairly good for eleven days, then good. No nervous upsets but cried a great deal on October 14. | 9/17, 9/20, hexamethyl- enamin | None. | |
| 39 | None..... | No mental disturbance at any time. Appetite always good | None..... | None. | |
| 40 | After three weeks. Made good recovery. | Appetite good from start. Only fairly so during relapse for the first three days. Then good again. No nervous symptoms. Somewhat sleepy. | | | |
| 41 | ? Had boil..... | Actively delirious on October 24; lasted about one week. Appetite very poor and very weak until October 28; then appetite improved but never very good. | | | |
| 42 | None..... | Appetite rather poor but no nervous disturbances..... | | | |
| 43 | None..... | Child was delirious and weak until early in November. Until November 19, the child did not have one comfortable night; after that slowly improved. | None..... | | 9/22, 50 million; 9/24, 50 million; 9/26, 100 million; 9/28, 100 million; 9/30, 150 million; 10/2, 200 million; 10/18, 20 c.c. horse serum; 10/19, 160, c.c. paternal blood; 10/20, 200 c.c. paternal blood 7 a. m.; 80 c.c. saline intravenously; 10/22, 1 p. m., 30 c.c. saline intravenously; 10/23, 20 c.c. horse serum; 11/13, 250 c.c. paternal blood intravenously. |

following the disease under the old methods of treatment. This nervous state was demonstrated to be a starvation psychosis. After a few days of forced feeding the boy came out of his stupor and delirium and became entirely rational. There is not the slightest doubt that most of the severe nervous symptoms noticed in the late stages of the disease heretofore were due to the starvation and the consequent increase in the toxemia.

Complications.—Pneumonia or bronchopneumonia were present in three cases, and in the only death that occurred the fatal issue proved by necropsy to be due to pneumonia.

Relapses.—Among our cases there were four relapses and one recrudescence, or a little over 10 per cent. Koplik and Heiman report 24 relapses among their 160 cases treated at the Mt. Sinai Hospital, a percentage of 15. Hand and Gittings had 4.8 per cent. of relapses in 145 cases.

Mortality.—There was one death, a mortality of about 2 per cent.

During the course of the fever, 60 per cent. of our patients gained in weight. This was the most remarkable fact about this series of cases; and is, in reality, the reason for this report. Heretofore the loss in weight has been very marked throughout the course of the disease, so that by the time the temperature has become normal, the patient has usually presented the picture of emaciation. The high caloric diet prevents this loss in the great majority of cases or reduces it to a very small amount. If we consider the weight of the patient at the time of leaving the hospital, it is found that 92 per cent. had gained in weight.

In 39 cases there was a gain in weight over that on admission as follows:

| Pounds | Cases | Pounds | Cases |
|----------------------|-------|-----------------------|-------|
| $\frac{1}{4}$ | 1 | 4 | 1 |
| $\frac{1}{2}$ | 1 | $4\frac{3}{4}$ | 2 |
| $\frac{3}{4}$ | 1 | 5 | 1 |
| 1 | 1 | $5\frac{3}{4}$ | 1 |
| $1\frac{1}{4}$ | 3 | 6 | 1 |
| 2 | 4 | $6\frac{1}{2}$ | 1 |
| $2\frac{1}{4}$ | 3 | $7\frac{1}{4}$ | 3 |
| $2\frac{1}{2}$ | 2 | $7\frac{1}{2}$ | 2 |
| 3 | 3 | 9 | 1 |
| $3\frac{1}{4}$ | 3 | $9\frac{3}{4}$ | 1 |
| $3\frac{1}{2}$ | 2 | $11\frac{1}{2}$ | 1 |

CONCLUSIONS

1. It is possible, in the great majority of cases, to feed children suffering from typhoid fever, even during the febrile period, with an amount of food furnishing sufficient calories to maintain or even increase their body-weight.

2. This high caloric diet, besides preventing the emaciation usual in this disease, greatly increases the comfort of the patient, prevents the severe nervous symptoms and lessens the dangers of the disease and of its complications.

THE ROENTGEN RAY IN THE DIAGNOSIS OF PULMONARY CONDITIONS IN CHILDREN *

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Although the importance of the Roentgen ray in the diagnosis of pulmonary tuberculosis has for some time been recognized, it is only within the last year that the possibilities of its use in the diagnosis of other pulmonary conditions has been developed.

Pneumonias showing few physical signs, due to their location and to the slight amount of lung tissue involved, serous and purulent exudates, abscess of the lung, hyperplasia of bronchial lymph-nodes, pneumothorax, as well as miliary tuberculosis, are now visibly demonstrated where formerly their existence was largely a matter of conjecture.

In the children's service at the Roosevelt Hospital, roentgenograms are taken of all pneumonias, not only in obscure cases for diagnosis, but also to determine associated conditions and the extent of active processes.

The cases reported illustrate the value of its aid in these various conditions.

The first roentgenogram (Fig. 1) shows a practically normal chest. The slight shadow at the right and left of the heart is called the hilum shadow and is due to the branching of the bronchi and vessels at the root of the lungs. In some cases the mediastinal glands are distinctly pictured.

In pneumonia the shadow in the lung tissue is produced by the congestion and hepatization there present. Many of these conditions are better shown in the negative than in the prints.

CASE 1.—Pneumonia. Philip O'D., aged 10 years. Admitted August 6, discharged Aug. 20, 1913. Family and past history negative.

Present Illness.—Four days ago complained of headache, referred to the frontal region, pain in the epigastrium and in the lower right chest, worse on inspiration. Has had cough and bloody expectoration. Vomited five or six times; bowels have been loose; anorexia.

Examination of the Lung: Good respiratory excursion, respiratory murmur is accentuated over the right lower chest anteriorly. No adventitious sounds heard.

On admission temperature was 101, respirations 28, pulse 140. Temperature that night rose to 104 and remained at 104 with slight remissions for three days when it fell by crisis to normal.

* Received for publication Feb. 4, 1915.

* From the Bliss Ward, Pediatric Service of the Roosevelt Hospital.

| Blood Examination | Aug. 6 | Aug. 8 |
|-----------------------------|--------|--------|
| White blood corpuscles..... | 40,000 | 27,400 |
| Polymorphonuclears | 94 | 87 |
| Lymphocytes | 6 | 8 |
| Hemoglobin | 95 | |

August 8.—Still has harsh and sibilant breathing over right anterior chest, but no definite signs of pneumonia. Roentgenogram (Fig. 2) shows partial consolidation of the right upper lobe, with extensive involvement of the middle lobe.

August 9.—Physical signs show typical bronchial voice and breathing over the right upper and middle lobes.

CASE 2.—Pneumonia.—Harold W., aged 7 months. Admitted July 21, discharged July 31. Family history negative.

Present Illness.—Breast fed for six months, then given milk and barley water. Four days ago began to cough and soon developed a high fever. Had one convulsion lasting twenty minutes, very dyspneic. Another convulsion on the day of admission. Marked rachitis.

Examination of the Lungs: Over the left posterior chest dulness with many coarse râles. On both sides friction rubs are heard. Temperature on admission 102, rising to 104, and ranging between 100 and 103 for three days, falling to normal on the fifth day. Respirations 36 to 80, pulse 130 to 160.

Blood examination:

| | |
|--------------------------|--------|
| White blood cells | 13,100 |
| Polymorphonuclears | 40 |
| Mononuclears | 9 |
| Hemoglobin | 60 |

Lumbar puncture: fluid not under pressure:

| | |
|--------------------------|-----------|
| White blood cells | 30 to cm. |
| Polymorphonuclears | 65 |
| Lymphocytes | 33 |
| Mononuclears | 2 |

Roentgenogram (Fig. 3) three days after admission showed a pneumonia involving the upper right and left lobes extending to the right middle lobe.

CASE 3.—Pneumonia. Woodford, aged 15 months. Admitted July 28, discharged Aug. 18, 1913. Father died of tuberculosis.

Present Illness.—Breast fed for seven months, then given modified milk and light diet. Three days ago the patient developed fever accompanied by a slight cough. For two days past the child has refused to lie on the right side. No history of chill.

Examination of the lungs: Anteriorly on the right side there is dulness from the supraclavicular space to the base, with bronchial voice and breathing down to the fourth rib. Left side of chest is clear.

Temperature 102, rising to 104. 4 in the afternoon. Respirations 80. Pulse 72. Temperature fell gradually to 100 with slight evening exacerbation. Patient developed a double otitis media and left the hospital against advice.

Two days after admission the Roentgenogram (Fig. 4) showed a pneumonia involving nearly all of the right side.

CASE 4.—Miliary tuberculosis. James S., aged 10 months. Admitted Oct. 14, 1913, died Oct. 15, 1913. Family history negative.

Present Illness.—Patient had been under observation in the outpatient department for over one month, brought first because of a swelling on the left side of the neck and also suffering from an enteritis. At this time the examination of the lungs shows many coarse râles widely distributed. The cervical adenitis responded very slowly to treatment and the child lost weight rapidly. The baby

was taken to the country but failed to improve. He was admitted to the hospital with a temperature of 100, respirations 56, pulse 156.

Examination of the Lungs: Chest normal contour, no rosary present, respiration somewhat limited over the right side and labored. Over the whole of the right chest are heard many mucous râles. There is dulness and marked increase in the voice and breathing in the axilla, extending upward over the middle and upper lobes. Behind there are showers of large moist râles over the entire chest, more concentrated at the apices.

Temperature rose that evening to 102.8, falling in the morning to 98.

Blood examination:

| | |
|--------------------------|--------|
| White blood cells | 10,700 |
| Polymorphonuclears | 75 |
| Lymphocytes | 11 |
| Mononuclears | 4 |
| Hemoglobin | 48 |

The roentgenogram (Fig. 5) showed both lungs studded with miliary tubercles. After death the peritoneal glands were easily palpable.

CASE 5.—Miliary tuberculosis. Philip M., aged 2 years. Admitted July 19, discharged July 31, 1913. Family history negative.

Present Illness—One month ago had measles followed by chicken-pox which lasted for two weeks, when he developed a high fever and a cough. Has had no night sweats, but has lost considerable weight.

Examination of the Lungs: In front many fine and coarse râles are heard over the entire chest. Behind there is dulness on both sides extending down as far as the spine of the scapula. Over the entire posterior chest are heard many fine râles. There is no change in the voice and breathing.

Temperature ranged from 101 to 104 in the evenings. Respirations 60 to 70. Pulse 160 to 180.

Blood examination:

| | |
|--------------------------|--------|
| White blood cells | 21,900 |
| Polymorphonuclears | 54 |
| Lymphocytes | 30 |
| Mononuclears | 15 |
| Eosinophils | 1 |
| Hemoglobin | 78 |
| Von Pirquet positive. | |

Roentgenogram (Fig. 6) showed many small areas apparently miliary tubercles over both chests.

Condition unimproved at discharge.

CASE 6.—Bronchopneumonia with serous exudate. Alexander M., aged 10 months. Admitted September 24, discharged Oct. 28, 1913. Mother is in the hospital at present with lobar pneumonia. Mother and child were admitted on the same day.

Present Illness.—Three days ago child was taken to a dispensary where a diagnosis of bronchitis was made. Chief complaint has been cough accompanied by high fever.

Examination of the Lungs: Slight dulness of the right base behind. Temperature ranged from 100 to 104 in the afternoons for four days when it fell to normal. Respirations 28 to 60.

Roentgenogram (Fig. 7) showed a bronchopneumonia with exudate involving the right side. A week later there was a reinfection with marked dulness and diminished breathing at the right base, causing a temperature which ranged from 98.8 to 105 for four days. Complicating this was a double otitis media and a general furunculosis which gradually subsided.

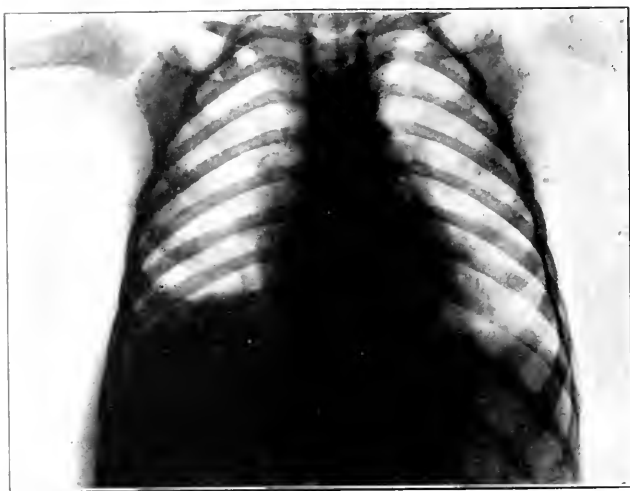


Fig. 1.—Practically normal chest. The slight shadow at the right and left of the heart, the hilum shadow, is due to the branching in the bronchi and the vessels at the root of the lungs.



Fig. 2.—Case 1, pneumonia. The house physician reports that this case was first seen by the surgeons because of the severity of the abdominal pain which radiated to the right lower quadrant. The diagnosis rested between an acute catarrhal appendicitis and a developing pneumonia. The patient was finally referred to the medical service and was of unusual interest as the physical signs did not correspond with the clinical severity of the attack. It was several days after the picture had shown an involvement of the right upper and middle lobes that these signs corresponded with a lesion of such extent.

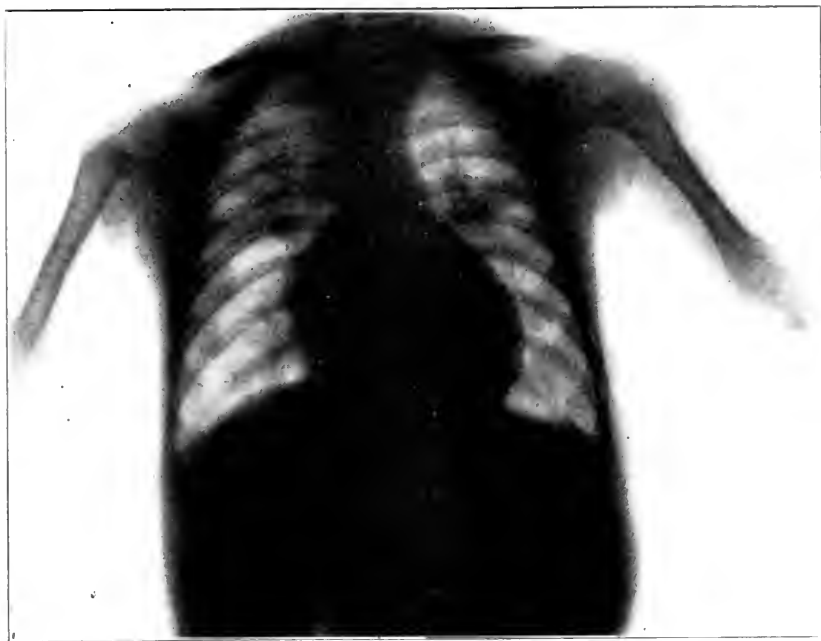


Fig. 3.—Case 2, pneumonia. When first seen this patient appeared to be suffering from some severe form of cerebral irritation. The child's head was thrown back; the respirations were exceedingly rapid, from 60 to 80 most of the time. Physical signs did not indicate the pneumonic areas involved and a meningeal condition was suspected. Lumbar puncture did not confirm this possibility. A roentgenogram showed distinctly a developing pneumonia, the signs of which soon appeared.



Fig. 4.—Case 3, pneumonia. The extent of the pneumonia is clearly shown. The physical signs at the time the picture was taken were very definite.

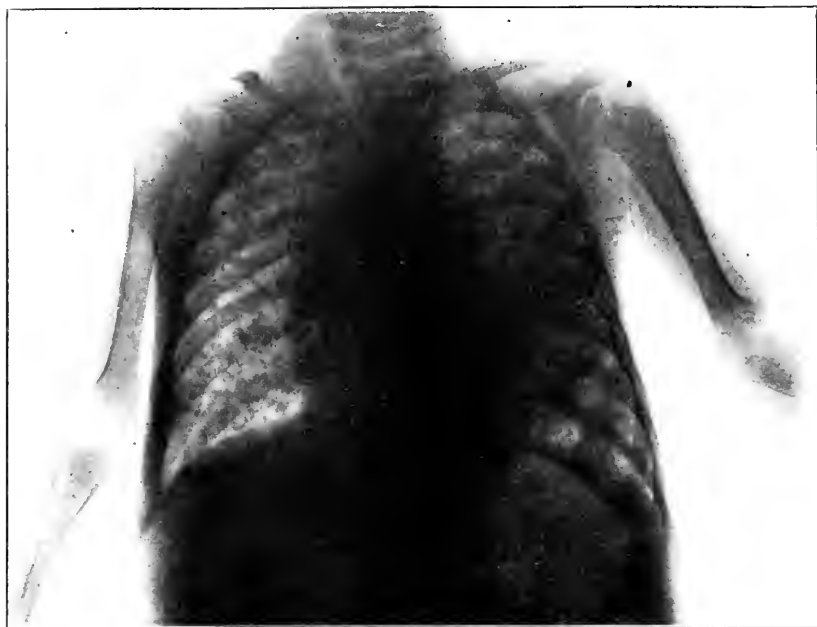


Fig. 5.—Case 4, miliary tuberculosis. Both lungs studded with **miliary** tubercles.

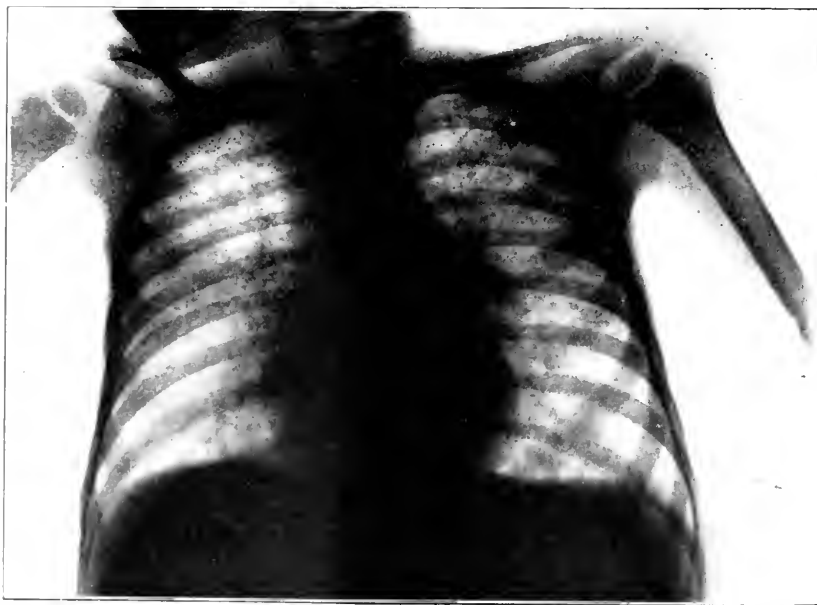


Fig. 6.—Case 5, miliary tuberculosis. It was thought on admission that the child might be suffering from a diffuse bronchopneumonia. The general course of the disease with the physical signs and the roentgenogram pointed clearly to a pulmonary, and probably a general, miliary tuberculosis.

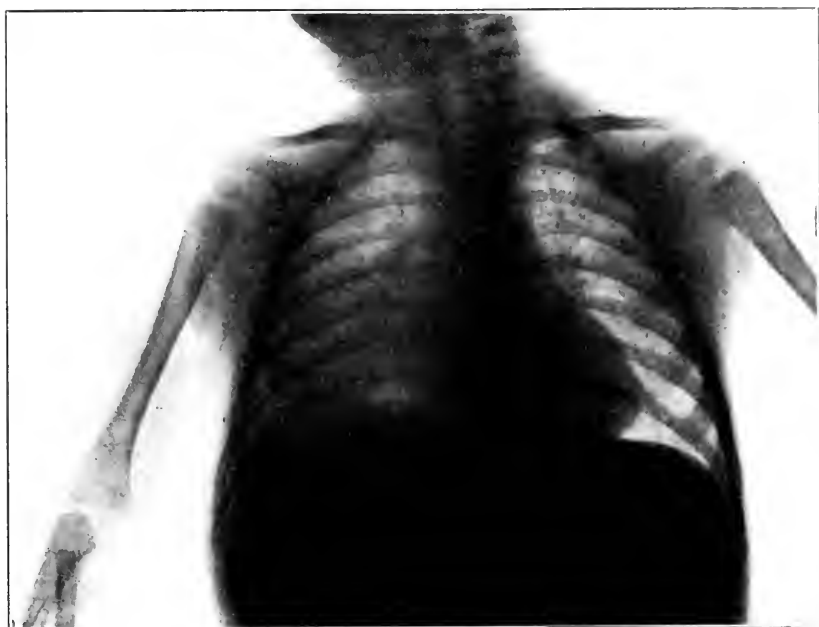


Fig. 7.—Case 6, bronchopneumonia with serous exudate. This picture shows very well the obliteration of the costal-phrenic angle on the right side, indicating the presence of exudate. No free fluid was found on paracentesis of the chest. The physical signs gradually disappeared, so it was concluded that the exudate had been absorbed. The child was discharged in good condition.

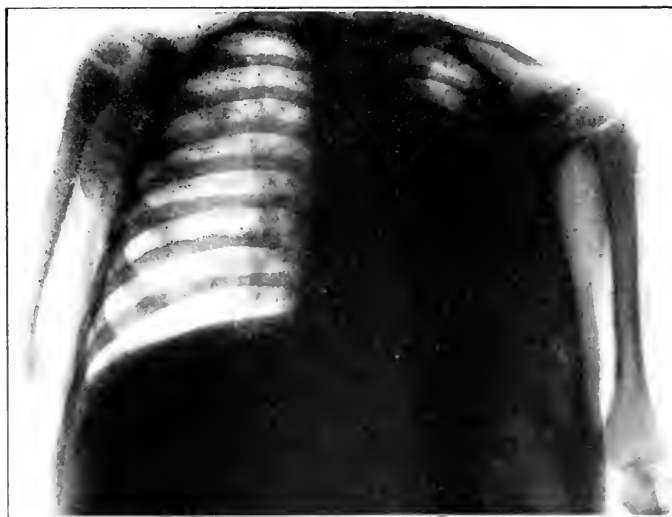


Fig. 8.—Case 7, abscess of the lung. This picture also shows the obliteration of the costal-phrenic angle on the left side. The diagnosis of empyema was made from the general physical signs and from the condition of the child. Although no pus was found at the time of the operation, it was felt certain that the lung was infected and consequently the wound was left open with drainage. The result showed that this conclusion was correct.

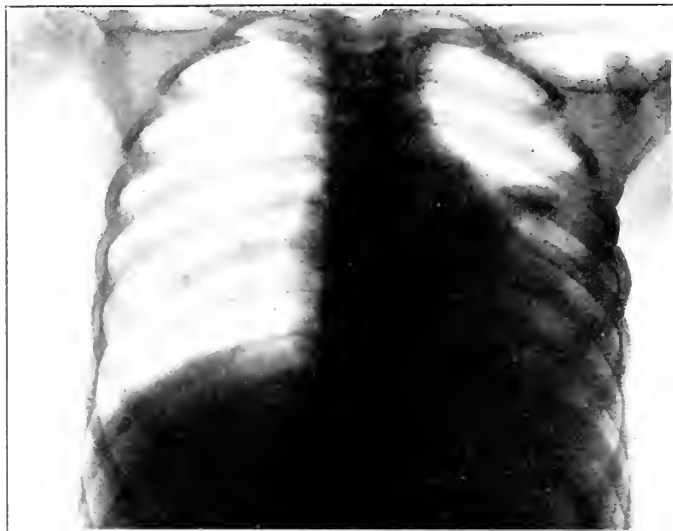


Fig. 9.—Case 8, abscess of the lung. July 12: Distinct shadow extending from the middle of the left chest to the base. There is a darkened area near the top of the shadow.

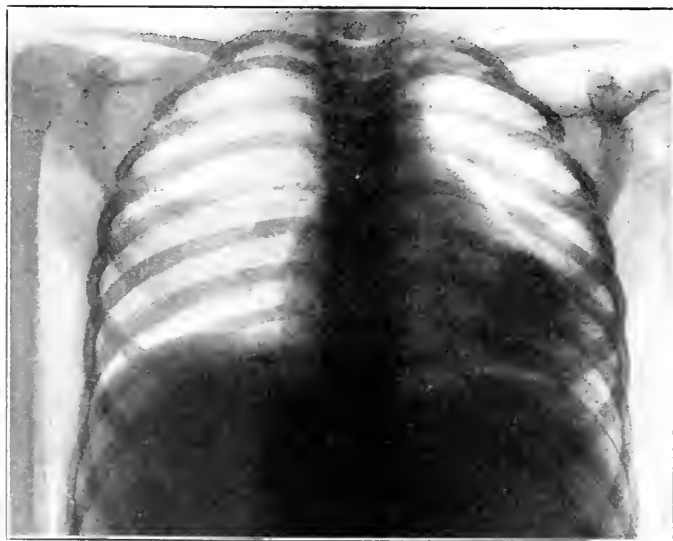


Fig. 10.—Case 8, abscess of the lung. July 22: Condition about the same, physical signs about the same. Area about the size of a dollar well defined.

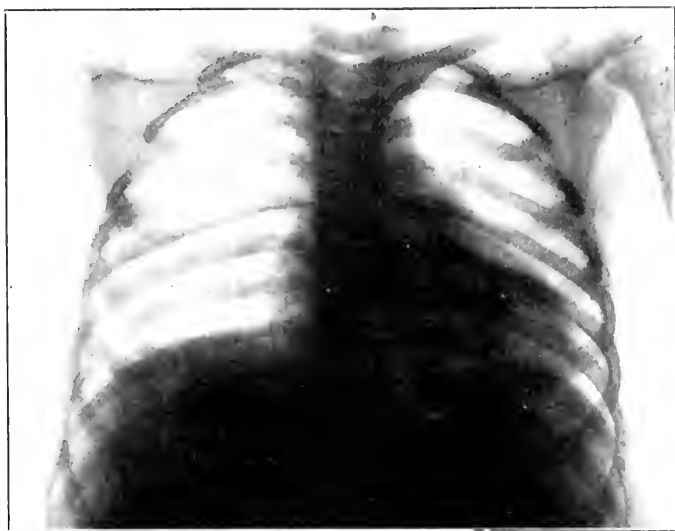


Fig. 11.—Case 8, abscess of the lung. July 31: Area is smaller and less distinct. The signs in the chest have nearly disappeared.



Fig. 12.—Case 9, pyopneumothorax. This shows very well the sacculated area of exudate with air above it. A thick band of adhesions apparently extends upward over the pocket. There is involvement of the lungs on both sides.



Fig. 13.—Case 9, pyopneumothorax. This picture is taken with the patient on her side and shows the change in the position of the air and exudate.



Fig. 14.—Case 9, pyopneumothorax. In this picture the sinus leading to the pocket is injected with bismuth.

| Blood Examination | Sept. 30 | Oct. 2 |
|--------------------------|----------|--------|
| White blood cells | 35,400 | 34,500 |
| Polymorphonuclears | 71 | 78 |
| Lymphocytes | 23 | 13 |
| Mononuclears | 6 | 9 |
| Hemoglobin | 52 | |

CASE 7.—Abscess of the lung (Fig. 8). Daniel D., aged 2 years. Admitted Oct. 29, discharged Dec. 31, 1913. Past history negative.

Present Illness.—Four months ago had pertussis followed one month later by a pneumonia complicated by a hydrothorax. This was treated by medicine and the condition was reported improved, although patient still suffered from occasional attacks of fever. Cough has been progressively worse. Child was taken to the outpatient department where a diagnosis of empyema was made.

Examination of the Lungs: Entire left chest, front and back, flat on percussion, absence of breath sounds.

| Blood Examination: | Oct. 30 | Nov. 21 |
|--------------------------|---------|---------|
| White blood cells | 17,000 | 38,000 |
| Polymorphonuclears | 72 | 76 |

Thoracotomy. No pus found in the pleural cavity, drainage tube left *in situ*. Three days later profuse discharge which continued for twenty-four days. Patient discharged on sixty-third day, wound closed. Normal breath sounds and resonance. Temperature for the first week ranged between 101 in the mornings to 103 to 104 in the afternoons, falling to 101 in the third week with slight exacerbations, and reaching normal in the fourth week.

CASE 8.—Abscess of the lung. Mary U., aged 6 years. Admitted July 10, discharged Aug. 18, 1913. Has had convulsions, measles, scarlet fever, pertussis and varicella.

Present Illness.—Three weeks ago tonsils and adenoids were removed. Following the operation there developed a high fever accompanied by a severe cough, which was often relieved by vomiting. The vomitus was brownish-yellow with a foul odor and was accompanied by a putrid expectoration. Mother thinks that the child has lost about six pounds in weight during the last ten days. For the past week patient has complained of severe pain in the left chest. At night there has been high fever.

Examination of the Lungs: In the left axilla, extending from the angle of the scapula to the base, there is dullness, absence of fremitus, voice and breathing.

Temperature on admission was 102, respirations 56, pulse 140. For the first three days the temperature ranged from 102 in the morning to 103 in the evening. It then fell to 101 with slight morning remissions for four days, after which it gradually became normal. The cough, which was very severe, occurred in paroxysms and was generally accompanied by foul-smelling vomitus or expectoration. After the cough often cavernous breathing could be heard over an area about the size of a dollar just below the spine of the scapula.

| | |
|--------------------------|--------|
| Blood examination: | |
| White blood cells | 20,800 |
| Polymorphonuclears | 78 |
| Mononuclears | 5 |
| Eosinophils | 1 |
| Hemoglobin | 74 |

Sputum Examination: Mucopurulent, few pus cells, few bacteria; no tubercle bacilli.

The course of the case is shown in Figures 8, 9 and 10. July 31, the date on which Figure 11 was taken, there was very slight cough and the patient had gained a pound in weight.

October 23: Patient has been very well since leaving the hospital and has gained six pounds in weight. Has very little cough or expectoration. Still has cavernous breathing at times just below the spine of the left scapula.

CASE 9 (Supplementary Case).—Pyopneumothorax (Figs. 12, 13 and 14). Through the courtesy of Dr. John Thacher the following case is reported from the adult medical service. M. P., female, aged 40 years. Admitted Nov. 21, 1912, discharged Jan. 22, 1913. Chief complaint, shortness of breath for the past seventeen days.

Present Illness.—For the past seventeen days patient has suffered from shortness of breath, pain in the chest accompanied by a severe cough. Two days ago the pain became more intense, especially on the left side, and the dyspnea increased.

Examination of the Lungs: Marked bulging and immobility of the entire left chest; right chest, $17\frac{1}{8}$ inches; left chest, $17\frac{1}{2}$ inches. No expansion on the left side. On this side fremitus is present over the root of the bronchi in front and behind, elsewhere absent. Hyperresonant tympanic note is heard on percussion over the upper left chest in front and behind with dullness and flatness below. Breathing is distant and diminished with a slightly amphoric quality in the first space and in the supraclavicular triangle. Elsewhere it is completely absent. Occasional râle is heard. At the angle of the scapula voice has an exaggerated nasal quality; below this it is markedly diminished. Hippocratic succussion is present. Right chest shows dullness at the right apex, in front and behind, with bronchovesicular voice and breathing. Fremitus is increased and a few subcrepitant râles are heard at the right base in the axilla and posteriorly.

Heart: Entire heart is markedly displaced to the right; apex beat is neither seen nor felt. On percussion the area of cardiac dullness extends $2\frac{3}{4}$ inches to the right of the midsternal line in the third space, and $1\frac{1}{2}$ inches to the left of the mid-sternal line in the fourth space. Maximum area of pulsation just below the ensiform cartilage, sounds are heard loudest over the ensiform. Action is regular, moderately rapid, sounds are distant but of fair quality. No accentuations or murmurs are heard. On admission temperature was 101.8, pulse 108, respirations 88. Patient very dyspneic, cyanotic, pulse of poor quality. Temperature ranged from 101.6 to 104 with morning remissions. Respirations 38 to 88. Pulse 108 to 130. On the second paracentesis, two days after admission, 450 c.c. of purulent exudate were withdrawn.

| Blood Examination: | Nov. 22 | Nov. 23 |
|--------------------------|-----------|---------|
| Red blood cells..... | 5,000,000 | |
| White blood cells..... | 14,800 | 22,200 |
| Polymorphonuclears | 76 | 76 |
| Lymphocytes | 24 | 24 |

Red cells pale, anisocytosis and poikilocytosis.

Patient was referred to the surgical service where she was operated upon and a partial osteotomy of the eighth rib was performed. Patient was discharged cured Jan. 22, 1913.

CONCLUSIONS

The Roentgen ray is of distinct value in the diagnosis of diseases of the respiratory tract. In pneumonia a shadow may appear over the suspected area several days before the development of definite physical signs.

It is of value in determining the progress of lung involvement. Roentgenograms may be taken on successive days as long as there are signs of active advancement of the process.

The Roentgen ray offers material assistance in differential diagnosis, tuberculosis, abscess of the lung, lobar and bronchopneumonia.

Through the obliteration of the costal-phrenic angle, the Roentgen ray indicates the presence of an exudate.

I wish to express my thanks to Dr. Freeman for permission to report the cases from the Bliss ward; to Dr. Thacher and to Dr. Sumner for their courtesy in allowing me to use the medical histories, and to Dr. Leaming, the radiologist of the hospital, for the excellent photographs and for suggestions regarding their interpretation.

50 Central Park West.

CASES OF EPIDEMIC CEREBROSPINAL MENINGITIS TREATED WITH FLEXNER'S ANTIMENINGITIS SERUM

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The following cases are placed on record because they show (1) the value of Flexner's antimeningitis serum in cases of epidemic cerebrospinal meningitis, even after the infection has lasted for many days or weeks; (2) the necessity for prolonged treatment in such cases, and on the other hand (3) the rapidity of cure when the serum is injected promptly after the manifestation of symptoms.

The first three cases reported were in children of one family.

CASE 1.—I. G., aged 8 months, was admitted to the hospital April 25, 1912. He was the youngest of four children. The onset of his present illness was April 16, 1912, with fever and irritability. When he was picked up he screamed with pain. After a continuation of these symptoms for five days, it was observed that he did not use his right arm. He remained fretful, his paralysis and fever continued, and for these reasons he was brought to the hospital, but chiefly because his sister, who was taken ill after him with a much more severe form of the disease, had already been admitted and had begun to show improvement from treatment. On examination in the ward (April 25, 1912), there was extreme hyperesthesia and he was exceedingly irritable. There was a paresis of the right arm, a *tache cérébrale* and exaggerated reflexes at the knee—*Kernig's sign was absent, the neck was not rigid and the anterior fontanel not bulging*—the temperature was 102.5 F. The leukocytes were 34,000.

Lumbar puncture No. 1 was done shortly after admission. Thirty c.c. of turbid fluid were removed and 20 c.c. of Flexner's serum were injected. The fluid was turbid and under increased pressure. The cells were mainly polymorphonuclear leukocytes and contained Gram-negative diplococci. The meningococcus was obtained from the fluid in culture. The Noguchi globulin reaction was positive. No unfavorable symptoms followed the injection of the serum.

The next morning (April 26, 1912) the temperature was 99 F., but as there was no other appreciable improvement in the child's condition, *lumbar puncture No. 2* was done; 20 c.c. of fluid were removed and 20 c.c. of serum were injected. The fluid was cloudy. There were many pus cells but no organisms were found. Culture showed no growth. After this injection the temperature rose to 105 F., but in twelve hours had fallen to 99 F.

The following day (April 27, 1912), as there was still no improvement in the general condition, *lumbar puncture No. 3* was done; 60 c.c. of fluid were removed and 15 c.c. of serum injected. The fluid was clear. There were very few pus cells and no organisms were found. There was a temperature reaction to 104 F. following this injection. The child showed improvement in the next twenty-four hours by being less irritable and less hyperesthetic. The right arm was still helpless, but the reflexes at the knee were not exaggerated. *Lumbar puncture No. 4* was done on this day (April 28, 1912); 15 c.c. of fluid were removed and 15 c.c. of serum injected. The fluid was clear and contained no pus cells or organisms. The temperature rose to 103 F. after this injection. The leukocytes were 15,000.

Lumbar punctures Nos. 5, 6 and 7 were done on the next three days and 20, 30 and 50 c.c. of clear fluid, respectively, withdrawn, containing no pus cells and no organisms. The punctures were performed in order to see if organisms were present, in which case serum was to be again injected, but also because each time, with a considerable accumulation of fluid, there was restlessness and irritability. These symptoms were at once relieved by withdrawing the excess of fluid. The child's improvement was marked, but as the temperature rose to 102 F. on May 2, 1912, lumbar puncture No. 8 was done and 20 c.c. of fluid were obtained. The fluid was cloudy and contained many pus cells. For this reason 20 c.c. of serum were injected, but no organisms were found and the

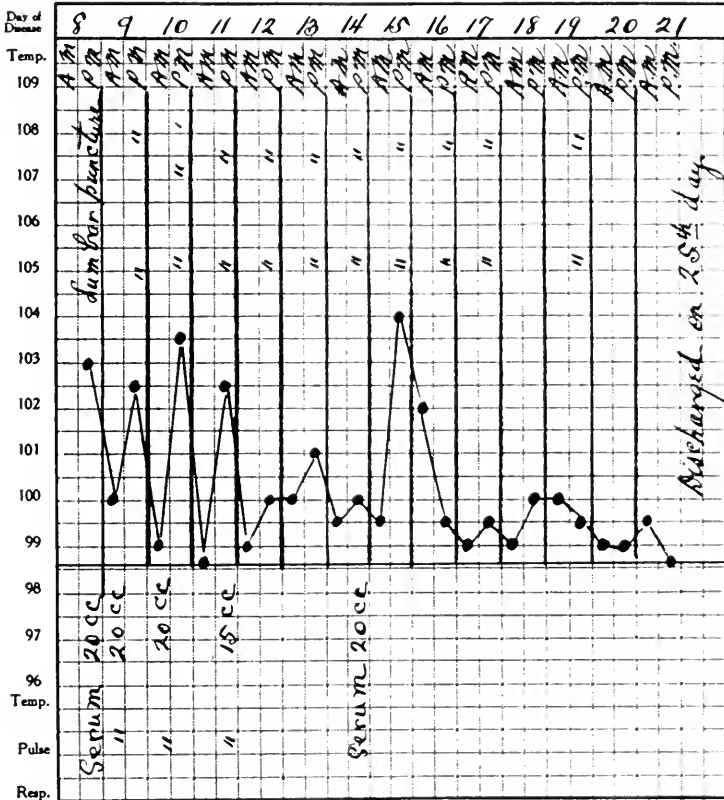


Chart 1.—Temperature curve in Case 1.

cultures were negative. The leukocytes were 24,000. The temperature rose to 104 F. after the injection. Lumbar punctures Nos. 9 and 10 made on the following two days showed slightly cloudy fluid with few pus cells, but no organisms. The Noguchi globulin reaction was still positive.

Lumbar puncture No. 11 was made two days later (May 6, 1912); 10 c.c. of fluid were obtained. This was clear. There were no pus cells and the Noguchi reaction was negative. The leukocytes were 12,000.

From this time the child improved rapidly. The temperature remained normal and the power in the right arm returned. He was discharged May 11, 1912, entirely well.

In this case the hyperesthesia, marked irritability of the child and the paresis of the right arm, were strongly suggestive of meningitis even in the absence of rigidity of the neck, Kernig's sign and bulging of the fontanel. It is interesting to observe that four days after the last injection of serum the spinal fluid became cloudy and that there were many pus cells but no organisms.

The reactions due to the serum were definite and sharp but were of short duration and entirely without sequelae.

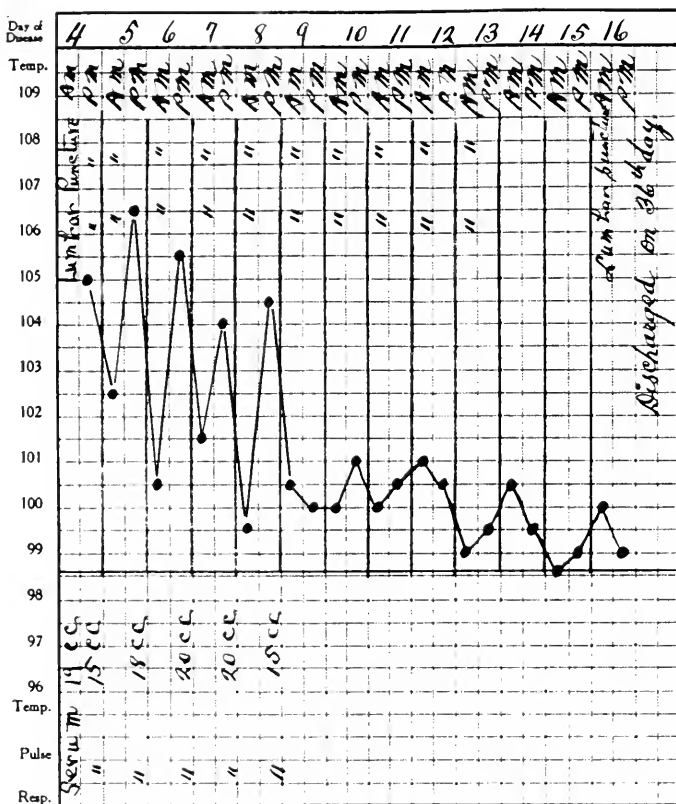


Chart 2.—Temperature curve in Case 2.

CASE 2.—F. G., aged 2½ years, was admitted to the hospital April 24, 1912. The onset of the present illness began April 20, 1912, four days after that of her brother (Case 1). She was taken acutely ill with fever, vomiting, headache in the left frontal region and convulsions. The next day (April 21, 1912) there was in addition a petechial eruption about the face and chest. Her condition remained the same during the next two days and on admission to the ward, April 24, 1912, she was stuporous and having one convulsion after another. There was slight rigidity of the neck muscles, internal strabismus of the right eye, a coarse tremor of the extremities, exaggerated reflexes, a *tache cérébrale*, a bilateral Babin-ski and a positive Macewen's sign. Kernig's sign was not present. The temperature was 105 F.; the leukocytes 28,000.

Lumbar puncture No. 1 was done at once; 20 c.c. of thick purulent fluid were withdrawn and 15 c.c. of Flexner's serum injected. The fluid showed many pus cells and Gram-negative intracellular diplococci. The meningococcus was obtained by culture. The Noguchi globulin reaction was positive. There was a severe reaction after the injection of the serum, as shown by the rise of temperature and an increase of the nervous symptoms. This lasted about one hour.

The child's general condition improved after the first injection and the next day, April 25, 1912, she could be aroused, the temperature was 101 F. and there were no convulsions.

Lumbar puncture No. 2 was done; 35 c.c. of fluid were withdrawn and 20 c.c. of serum injected. The fluid was turbid and contained many pus cells, but few organisms. The cultures were positive. After this injection of serum there was a severe reaction. The temperature rose to 107 F., the respiration was irregular and rapid and there was a coarse general tremor. No convulsions.

On the following day (April 26, 1912) the temperature was 100 F., and although she lay for the most part in a stupor she recognized her parents when aroused. The reflexes were not exaggerated and there were no convulsions. *Lumbar puncture No. 3* was done; 35 c.c. of fluid were removed and 20 c.c. of serum injected. The fluid was cloudy. There were many pus cells but only a few organisms. The organisms were extracellular. The cultures showed no growth. The Noguchi reaction was positive. There was the same severe reaction lasting for about one hour after this injection.

April 27, 1912, although the child was in every respect improved, *Lumbar puncture No. 4* was done; 35 c.c. of fluid were obtained and 20 c.c. of serum injected. The fluid was clear, containing only a few pus cells and no organisms. The Noguchi reaction was positive. The reaction after this injection was not severe except for the high temperature.

Lumbar puncture No. 5 was done April 28, 1912; 20 c.c. of clear fluid containing no organisms were obtained; 15 c.c. of serum were injected. The Noguchi reaction was negative. *Lumbar puncture* was done the five days following. Twenty to 70 c.c. of clear fluid containing no pus cells or organisms were obtained. After an interval of two days 80 c.c. of clear fluid were obtained by *lumbar puncture No. 11*. This fluid showed no pus cells or organisms. The Noguchi reaction was negative. The indications for the repeated withdrawal of fluid were the same as with the first child. The child improved rapidly after the fifth injection of serum. The temperature varied between 99 F. and 101 F., gradually becoming normal. The leukocytes fell to 12,000 and except for a serum rash ten days after the first injection of serum, the convalescence was uneventful. During convalescence lumbar punctures, four in all, were done at intervals. Each time from 10 to 30 c.c. of clear fluid were obtained.

The case was a severe one. Four days after the onset the child was in a stupor, the temperature was very high and she was having frequent convulsions.

CASE 3.—M. G., aged 6 years, was taken ill April 26, 1912, at noon, ten days after her brother (Case 1). The onset was acute, with vomiting, frontal headache and fever. She was admitted to the hospital four hours later (4 p. m., April 26, 1912) after having had several convulsions. On admission the temperature was 103 F., there was drowsiness and she complained, when aroused, of intense headache. On examination there was a *tache cérébrale*, slightly exaggerated reflexes and dilated pupils. Macewen's sign was present. There was no rigidity of the neck muscles, nor was Kernig's sign present. The leukocytes were 30,000.

Lumbar puncture No. 1 was done at once; 25 c.c. of fluid were withdrawn and 20 c.c. of Flexner's serum injected. The fluid was clear but contained, after centrifugation, a few pus cells and Gram-negative intracellular diplococci. The cultures showed meningococci. The Noguchi globulin reaction was positive.

The following day (April 27, 1912) there was a fine petechial eruption on the upper part of the chest and neck. The patella tendon reflexes were markedly exaggerated and Kernig's sign was present. In other respects, however, there had been a marked improvement. The temperature was lower (100 F.) and the child was much brighter and complained no longer of headache. Lumbar puncture was not done. From this day improvement was rapid. The temperature remained normal and the number of leukocytes fell to 12,000 (May 7, 1912). Convalescence was uneventful except for the appearance of an urticarial eruption on the seventh day and the child was discharged May 7, 1912, eleven days after the onset of the disease.

These three cases show almost with the nicety of a carefully planned experiment the value of the serum treatment and the rapidity of its effect in direct proportion to the time of its employment. Children

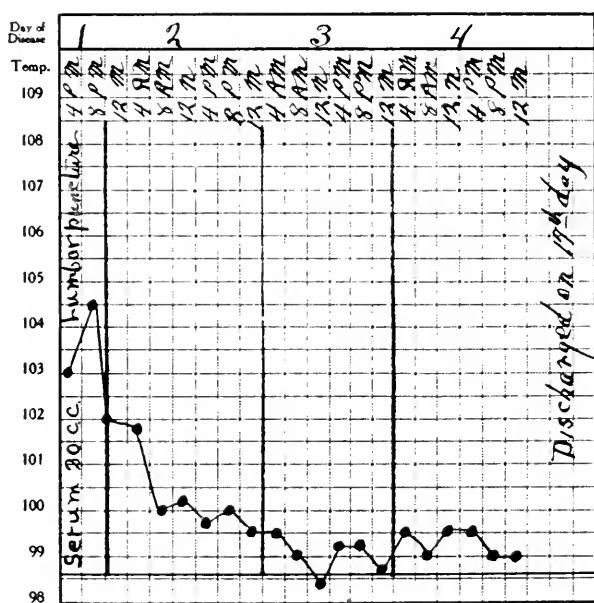


Chart 3.—Temperature curve in Case 3.

1 and 2 had been ill nine and four days, respectively, before the institution of treatment. Both were severely ill, the second child particularly so. In both the disease yielded to treatment, but only after many days and repeated injections of the serum. In marked contrast is the case of Child 3, a member of the same family. Her disease was marked by a sudden and severe onset, yet it yielded promptly and permanently to only one injection of the serum. I know of no similar recorded case in which treatment was begun so soon (four hours) after the beginning of symptoms. The temperature charts show graphically this distinction. Of particular interest was the fact that the duration of the disease was so short that the cerebrospinal fluid had not yet

become turbid. Such a fluid though unusual is occasionally encountered. The presence of meningococci, together with the perfectly characteristic nervous symptoms and the petechial eruption, leave no doubt of the diagnosis. Unless other children in the same family had previously suffered from similar symptoms, it is likely that hours or days would have elapsed before serum treatment would have been possible.

The two following cases are examples of prolonged meningococcus meningitis showing no tendency to improve, but yielding at once to the serum:

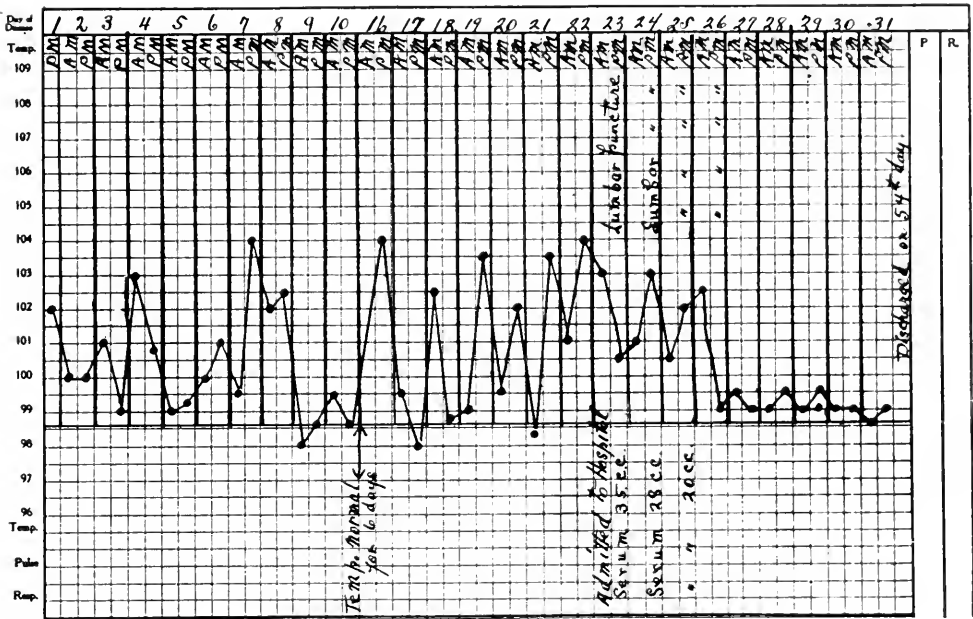


Chart 4.—Temperature curve in Case 4.

CASE 4.—L. A., aged 4 years, was admitted to the hospital May 23, 1912. The present illness began April 30, 1912, with fever, convulsions and headache. The temperature varied intermittently from 97 to 104 F. and the convulsions continued at irregular intervals until May 9, 1912. Then the temperature remained normal and he was up and about the house until May 15, 1912, a period of six days. On the fifteenth he had a convulsion and the temperature rose to 104 F. The intermittent temperature and convulsions continued and he was admitted to the hospital May 23, 1912, twenty-three days after the onset of the disease.

On examination in the ward he was found to be greatly prostrated, emaciated, irritable and complained of a severe headache. There was marked hyperesthesia, rigidity of the neck, exaggerated reflexes, ankle clonus and a positive Kernig and Macewen sign. At night he had a shrill meningeal cry; the temperature was 103 F. The leukocytes were 24,000. Lumbar puncture No. 1 was done; 25 c.c. of fluid were withdrawn. The fluid was cloudy and

contained pus cells and many Gram-negative intracellular diplococci. Cultures showed meningococci. The Noguchi globulin reaction was positive; 25 c.c. of Flexner's serum were injected six hours later. During the injection of the serum the child complained of severe pain in the legs and the temperature which was 97 F. afterwards rose to 103 F.

The next day, May 24, 1912, he showed improvement by being less hyperesthetic and less irritable. The temperature remained high. *Lumbar Puncture No. 2* was done; 50 c.c. of fluid were removed and 40 c.c. of serum were injected. The fluid was slightly cloudy and contained few pus cells, but no organisms. The Noguchi reaction was positive.

Lumbar puncture No. 3 was done May 25, 1912; 25 c.c. of fluid were withdrawn and 20 c.c. of serum injected. There was a reaction in the temperature to 103 F. The fluid removed at this time was collected in four test tubes. It flowed freely from the needle, and though clear, had a peculiar yellow hue. It was taken immediately, after the serum had been injected, to the laboratory, and there was found to have coagulated to the consistency of solid agar. There were no pus cells nor organisms. The cultures showed no growth.

Lumbar puncture No. 4 was done the next day, May 26, 1912. The fluid appeared in drops at the end of the needle and coagulated at once, and when a drop was wiped off another would appear and rapidly become coagulated. At this time the child showed marked improvement, the temperature remained normal, and except for a great weakness which continued to the time of his discharge (June 23, 1912) he made an uneventful recovery.

CASE 5.—E. T., aged 6 years, was admitted to the hospital Nov. 27, 1912. The present illness began three weeks previously (Nov. 7, 1912) when she complained of headache and feeling tired. She was in this state for about one week or until Nov. 15, 1912, when she had three general convulsions, each lasting about five minutes. After that she remained in bed with headache and an afternoon rise of temperature to 104 F. One week after this (Nov. 20, 1912) her neck became stiff. Since then she had had headache, afternoon fever and stiffness of the neck. She had not vomited. On admission to the ward she was conscious and complained of headache. There was extreme emaciation, the head was drawn back and the back arched. Macewen's sign was not present. The eye grounds were normal. The abdomen was boat-shaped. There was a bilateral Kernig, exaggerated reflexes and ankle clonus. The temperature was 100 F., the leukocytes 30,400.

Lumbar puncture No. 1 was done; 20 c.c. of fluid were removed and 20 c.c. of Flexner's serum injected. The serum was turbid and under increased pressure. There were many pus cells and Gram-negative intracellular diplococci and the Noguchi reaction was positive. The meningococcus was obtained by culture. After the injection the temperature rose to 104 F. The next day (Nov. 28, 1912) there was no improvement and *lumbar puncture No. 2* was done; 15 c.c. of fluid were removed and 20 c.c. of serum injected. The fluid was turbid and there were a few pus cells with a few Gram-negative intracellular diplococci. Cultures showed the meningococcus. The temperature fluctuated for the next few days from 99 F. to 104 F., but there was no improvement in the child's condition. *Lumbar punctures Nos. 3, 4 and 5* were done and 20, 40 and 15 c.c., respectively, of serum were injected. There was no growth on cultures and the fluid was clear after the second injection of the serum. The Noguchi reaction remained positive. After the fifth injection, Dec. 1, 1912, the temperature remained normal. The child's general condition was improved and she could move her neck freely from side to side. The retraction continued but was less marked. Dec. 5, 1912, the temperature rose to 103 F., and though she seemed in as good condition as before, *lumbar puncture No. 6* was done; 30 c.c. of fluid were removed and 30 c.c. of serum injected. The fluid was clear; there were no pus cells or organisms. The cultures were

negative and the Noguchi reaction was negative. The rigidity of the neck became less and less, disappearing about Dec. 11, 1912. Convalescence was slow and she was discharged Dec. 26, 1912.

DISCUSSION

These five cases varying in duration from four hours to twenty-three days were all favorably influenced by the antimeningitis serum. All the patients recovered without sequelae. A study of these prolonged

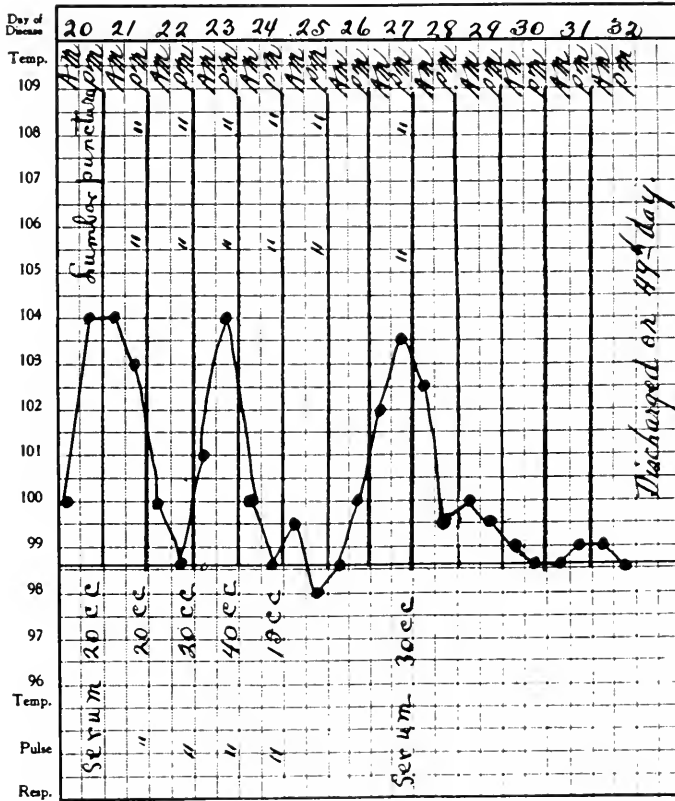


Chart 5.—Temperature curve in Case 5.

cases shows the necessity of repeated injections of the serum and of continuing the withdrawal of cerebrospinal fluid at frequent intervals well after the fluid is clear and no organisms are to be found microscopically or by culture. The nervous symptoms and their prompt amelioration after lumbar puncture make this clear. That such large quantities as 20 to 80 c.c. of fluid can be withdrawn shows that temporarily the injury to the meninges prevents the absorption of the fluid which is undoubtedly formed in excess owing to inflammatory irritation of the choroid plexus.

Occasionally the fluid may exhibit unexpected and peculiar characteristics, as in Case 4, in which spontaneous coagulation took place, and in Case 1, in which in convalescence a cloudy fluid due to polymorphonuclear leukocytes appeared without any cocci or other organisms being present and following several findings of perfectly clear fluid.

The reactions due to the repeated injections of foreign serum were marked. There was frequently high fever and restlessness, but these were of short duration.

These cases while few in number serve nevertheless to emphasize the fact that in any case of meningococcus meningitis, no matter of what duration, provided viable meningococci are present, Flexner's antimeningitis serum should be used repeatedly, and that even in apparently unfavorable cases, complete recovery may occur.

The first four cases were observed in the St. Louis Children's Hospital in the service of Dr. Howland, and I am further indebted to him for the opportunity of reporting the fifth case.

122 West Lockwood Avenue.

A STUDY OF 105 CASES OF TUBERCULOUS MENINGITIS*

ALFRED EDWARD MEYERS, M.D.

SAN FRANCISCO

Most of the leading text-books on pediatrics give very good composite pictures of tuberculous meningitis, but, as in many of the other diseases, one rarely sees the whole picture in any one case. Nor has he any idea of the relative frequency of the various signs and symptoms of the disease. It was the intention, in the analysis of these cases, to present everything that appeared in the histories, thereby giving an idea of the disease as it appears on the records of the Children's Hospital in Boston. The analysis comprises all the cases which were admitted to the hospital since January, 1910, which takes it back before a few of the later signs of meningitis were known. Most of the signs are more or less present at some stage of the disease, and it is interesting to note at just which stage any particular sign appears and disappears. Many of the records are complete, and while in not a few of the cases neither the organism nor the necropsy was obtained, yet the diagnoses were unquestionable from the clinical picture and were made by competent men.

Sex.—Of the 105 patients, 53 were females and 52 were males, the youngest being 5 months old and the oldest 11 years. Over 30 per cent. were between the ages of 2 and 3 years, while over 56 per cent. were between the ages of 2 and 5 years and over 80 per cent. between the ages of 18 months and 5 years (see Chart 1). This is interesting from the fact that most of the other observers have recorded the ages up to 3 years of age, while Chart 1 shows the relative frequency up to 12 years of age, which is the age limit in the Children's Hospital. No case occurred in patients under 5 months or over 11 years in the series. Holt's¹ largest number came between the ages of 9 and 12 months (20 per cent.).

Seasonal Prevalence.—Holt, in 1911, showed that the seasonal prevalence for tuberculous meningitis in New York, was in the month of April, 16 per cent. of his 218 cases occurring in that month. Recording all the cases which were admitted into the Children's Hospital for the last ten years, a total of 273 cases, Boston's highest number occurred

* Received for publication Feb. 25, 1915.

* This work was done at the Children's Hospital, Boston, during the service of the late Dr. T. M. Rotch.

1. Holt, L. Emmett: Observations on Three Hundred Cases of Acute Meningitis in Infants and Young Children. *AM. JOUR. DIS. CHILD.*, January, 1911, p. 26.

during the months of June, 12.3 per cent., July, 11.3 per cent., and January, 11 per cent., while April produced only 9.5 per cent. October and November produced the lowest number, 5.8 per cent. (see Chart 2). Computing the seasonal prevalence for the last four years, as seen in Chart 3, the largest number occurred during the month of January, 15.2 per cent., followed by the month of April with 10.5 per cent., and July, 9.5 per cent., while the lowest percentage occurred during the months of September, October and November, 5.7 per cent. Up to 1909 there had been a gradual increase in the number of cases recorded (Chart 4). Since that time there has been a gradual decline, undoubtedly due to the improved methods of sanitation, the reporting of all tuberculous cases, the influence of social service, in short, to the awak-

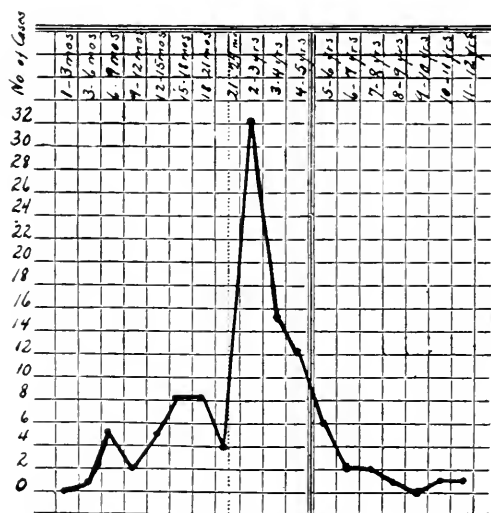


Chart 1.—Showing ages when the disease was contracted.

ened interest in tuberculosis. Tabulating the seasonal prevalence for babies under 16 months (Chart 5), there were more cases during the months of January and March than in any other month.

Previous Diseases.—Measles was mentioned in the past history of twenty-seven cases, or 26 per cent., and whooping-cough in 22 per cent. Other diseases mentioned in the histories were as follows: pneumonia, 11 per cent.; chicken-pox, 8 per cent.; bronchitis, 6 per cent.; diphtheria, 6 per cent.; mumps, 4 per cent.; otitis media, 4 per cent.; colds, 2 per cent.; Pott's disease, 2 per cent.; tuberculous osteomyelitis 1 per cent.; indigestion, 1 per cent.; abscesses, 1 per cent.; tuberculous lymph-nodes, 1 per cent.; coryza, 1 per cent.; malaria, 1 per cent. Some of the patients had had only one disease, while others had had four or five. Thirty-eight per cent. had had no previous mentioned diseases.

The most frequent combinations of previous diseases were: measles and whooping-cough in three cases, measles and pneumonia in three cases, and measles and chicken-pox in two cases. Other combinations were as follows: measles, chicken-pox, whooping-cough and suppurative adenitis; whooping-cough and diphtheria; measles, bronchitis and otitis media; whooping-cough, diphtheria and chicken-pox; whooping-

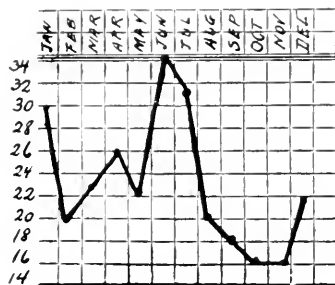


Chart 2.—Seasonal prevalence of 273 cases of tuberculous meningitis.

cough and adenitis; whooping-cough and bronchitis; whooping-cough, measles and mumps; whooping-cough, measles and pneumonia; whooping-cough, measles, mumps, bronchopneumonia, laryngeal diphtheria and otitis media; whooping-cough and pneumonia; measles, mumps and chicken-pox; measles, pneumonia and otitis media.

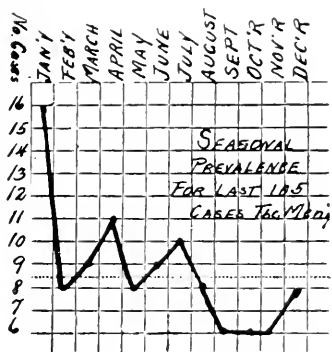


Chart 3.—Seasonal prevalence for last 105 cases tuberculous meningitis.

Duration.—Holt found that the average duration of the disease of children up to 3 years of age, from the time the child began to show signs of apathy, vomiting and slight temperature, was two and a half weeks. Rankin² gives twenty-three days as the duration for his series. The average duration of the disease found in this series of all cases of

2. Rankin, G.: Meningitis in Children. Brit. Med. Jour., London, 1910, i, 1045.

children up to 12 years of age, from the beginning of symptoms, was seventeen days, which is exactly the same as Holt reported for children under 3 years in New York. The shortest duration was five days, while the longest duration was forty-three days. Nearly 50 per cent. of all the patients were sick from ten to eighteen days (Chart 6). The duration seems to vary somewhat in the different ages. Chart 7 shows

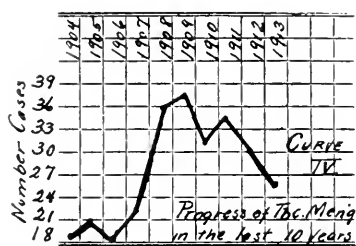


Chart 4.—Progress of tuberculous meningitis in the last ten years.

that the average duration of the disease is shorter in a child past 4 years of age, being greatest between the ages of 3 and 4 years (19.5 days) and shortest between the ages of 4 and 12 years (15 days).

Duration in the Hospital.—The average duration in the hospital was 5.8 days, the longest being 21 days and the shortest 12 hours. Only 14 per cent. of the patients lived 10 days or over in the hospital, and

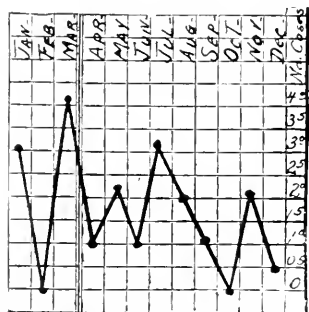


Chart 5.—Mortality under 16 months.

nearly 60 per cent. lived 5 days or less. Chart 9 shows that most of the patients lived 3 days. The duration of the disease is longer now than formerly, probably owing in part to the earlier diagnoses and repeated lumbar punctures. That the latter is true may be seen from Chart 8, the average duration in the hospital varying almost directly with the number of lumbar punctures, ranging from 10 to 14 days with five lumbar punctures, to 4.4 to 9.7 days with four lumbar punctures or

under. This fact lends support to Dunn's suggestion³ of early and repeated lumbar punctures as part of the treatment of tuberculous meningitis. In one of the very recent cases in the hospital the patient

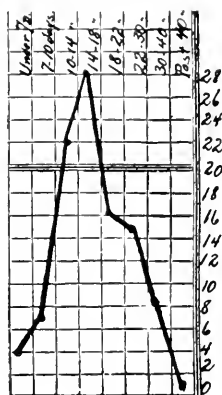


Chart 6.—Duration of disease.

had seven lumbar punctures and lived 15 days, having been sick 22 days outside the hospital. In the last ten cases in the hospital the patients had on an average 4.4 lumbar punctures each, while the average duration was 9 days. In thirty consecutive cases previous to these the

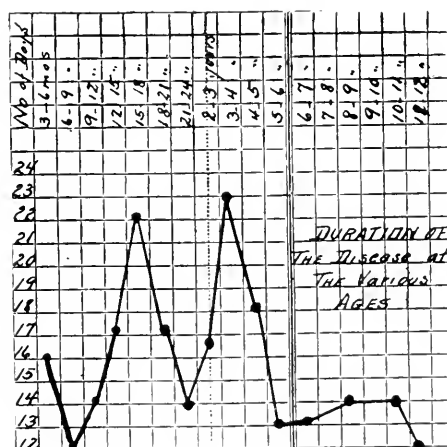


Chart 7.—Duration of the disease at the various ages.

patients had on an average 1.9 lumbar punctures, while the average duration was only 5.4 days.

Lumbar Punctures.—The largest number of lumbar punctures made in one case was seven, and the smallest one, puncture being often

3. Dunn, Charles Hunter: Cerebrospinal Meningitis, Its Etiology, Diagnosis, Prognosis and Treatment, *Am. Jour. Dis. Child.*, February, 1911, p. 95.

made simply for diagnosis. Lumbar puncture was done once in each of 58 cases, twice in each of 26 cases, three times in each of 6 cases, four times in each of 5 cases, five times in each of 8 cases, and seven times in each of 2 cases. Most of the patients receiving more than four lumbar punctures were the recent ones. Many of the patients seemed to brighten up after the withdrawal of spinal fluid, and in not

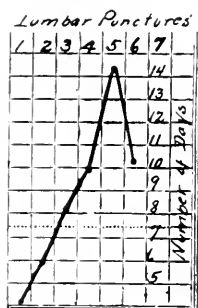


Chart 8.—Relation of number of lumbar punctures to duration.

a few cases there followed a remission of pulse and temperature. Convulsions in tuberculous meningitis at the present time in the hospital are almost unknown since spinal puncture has become part of the treatment of the disease. In no case was there any record of any harm having been done owing to the withdrawal of too much spinal fluid.

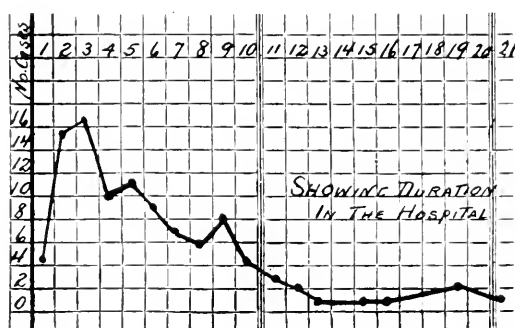


Chart 9.—Duration in the hospital.

The spinal canal was allowed to drain until the fluid ran at the rate of about ten or twelve drops per minute. In view of the two cases reported by Stiles⁴ before the International Congress on Tuberculosis at Washington in 1908 as undoubted cures, also the rapidity with which the spinal fluid recurs under this pathologic condition, the appar-

4. Stiles, C. W.: Proc. Sixth Internat. Cong. on Tuberculosis, Washington, 1908.

ent brightening of the patient after each lumbar puncture, the elimination of a certain amount of toxin, and also the fact that the spinal fluid in repeated punctures is generally under but very slight pressure, it would seem that there is but very little danger, if any, in removing too much spinal fluid from the canal. As a general rule, there is rarely any difficulty in holding a child as there is in doing a spinal puncture in the epidemic form, nor is there sufficient pain to justify the discomfort of anesthesia. Usually at the time when the child enters the hospital there is scarcely any rigidity of the spine, and the degree of apathy is so marked that it is a perfectly simple procedure to draw off

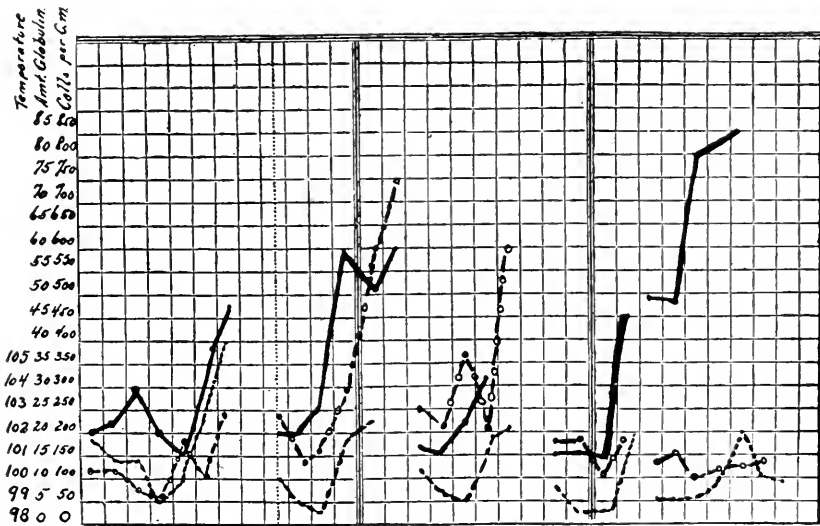


Chart 10.—Relation between amount of globulin, temperature and cells per cubic millimeter. Solid line denotes amount of globulin, dotted line, temperature and line composed of dashes and circles, cells per cubic millimeter.

from 20 to 30 c.c. of fluid as the case permits. Lumbar puncture is done in all cases once every forty-eight hours.

Organisms in the Spinal Fluid.—Several articles on the examination of spinal fluid in tuberculous meningitis have been published, in which it is reported that the organism has been found in practically every case. As a matter of fact, the finding of tubercle bacilli in spinal fluid resolves itself into a matter of time. With careful technic, it has been possible to demonstrate the organisms nearly every time in the first or second puncture, but the third or fourth puncture almost invariably shows them. The system in vogue then at the hospital was to centrifugize the fluid with water-power for from six to twelve hours. All but the last three or four drops of fluid plus the clot was drawn off with a long sterile dropper and thrown away. The clot and the remaining

fluid were then put on a cover-slip and teased out with fine sterile needles. This cover-slip preparation was then allowed to dry in the air, fixed, and then stained with carbol-fuchsin, decolorized with 20 per cent. sulphuric acid and counter-stained with Loeffler's methylene blue. Tubercle bacilli were found in 21.5 per cent. of this series of cases, and were found just as readily in infants as they were in older children. Seventeen per cent. of the cases were verified by necropsy, no organisms having been found, which was evidently the reason for necropsy. This makes a total of 38.5 per cent. which were found to be positively tuberculous. Hemenway⁵ notes that the last fluid withdrawn after the child is raised to the sitting position is the best to examine for organisms. This is probably due to the fact that the last part withdrawn seems to contain more fibrin than the first part. The relation of the first part of the spinal fluid to the last part will be taken up later.

Pressure and Clearness of Spinal Fluid.—The spinal fluid was under pressure in 80 per cent. of the cases recorded, varying all the way from very slight to very great pressure. In 11 per cent. of the cases the pressure was normal. In 9 per cent. it was not recorded. In most cases it appeared late in the disease. Where the pressure was normal the amount usually did not exceed 20 c.c. of fluid. The amount of pressure, as roughly gauged, bore no relation to the age or to the abolition or retention of reflexes. Broadly speaking, however, where there was no pressure, there was no or scarcely any disturbance of the reflexes. There was no relation between the amount of pressure and the presence of convulsions, bulging fontanelle or retraction of the head. Most of the fluid obtained was clear, few of the cases recording "very slight turbidity" or "contained small bits of fibrin." A few were recorded as blood-tinged, and one was contaminated by secondary infection. In no case was the fluid recorded as actually turbid. The average amount of fluid obtained was 25 c.c., and ranged from 5 c.c. to 75 c.c.

Cell Count.—The average cell count was 198 cells to the cubic millimeter, the lowest counts being 24, 26, 30, 35, 38, 48, and 50 cells, while the highest count was 960 cells. There was no relation between the cell count and the age, sex or amount of spinal fluid. Its relation to the globulin content of the spinal fluid and the temperature and the stage of the disease will be discussed under the head of globulin. The cell count seemed to bear some slight relation to the white blood count,

5. Hemenway, Josephine: The Constant Presence of Tubercle Bacilli in Cerebrospinal Fluid of Tuberculous Meningitis, AMER. JOUR. DIS. CHILD., January, 1911, p. 37.

for the average white blood count for all cases with cell counts over 350 cells, was 22,700, while the average white count for all cases with cell counts under 100 cells, was 17,000. The prevailing type of cell in the spinal fluid was the small mononuclear, ranging from 90 to 100 per cent. in 67 per cent. of the cases, and from 80 to 90 per cent. in 20 per cent. of the cases. In 4 per cent. of the cases the mononuclears ranged between 70 and 80 per cent., in 3 per cent. the mononuclears ranged between 60 and 70 per cent., and in 3 per cent. the mononuclears ranged between 40 and 60 per cent. There were only three cases in which the polymorphonuclear leukocyte was the prevailing type of cell, one recording 85 per cent. polymorphonuclears, and in two others "mostly all the cells were polymorphs."

Fibrin Clot.—A definite fibrin clot was present in 70 per cent. of the cases, absent in 8 per cent., and not mentioned in 22 per cent. The time of appearance of the clot varied from one to forty-eight hours. The clot seemed to form earlier in the last part of the spinal fluid than it did in the first part of the same puncture.

The Noguchi or Butyric Acid Test for Globulin.—A positive test for globulin was obtained in 50 per cent. of the cases; in 7 per cent. it was negative, and not recorded in 43 per cent. There is no doubt but that there is a positive globulin test in every case of tuberculous meningitis. In the 7 per cent. of negative results, there must have been an error in technic, or enough time was not given for the precipitation of globulin, or else there was a lack of familiarity with the normal globulin content of the spinal fluid. Normal spinal fluid, when treated with 10 per cent. butyric acid in normal saline, one to five parts, heated to boiling, will, on the addition of one part of normal sodium hydroxid, give a slight turbidity, which rarely precipitates on standing twenty-four hours. Tuberculous meningitic fluid will, in practically every case, give a precipitation almost immediately, especially if boiled after the normal sodium hydroxid is added. Some of the cases show only a slight increase over the normal, and if one is not in the habit of measuring the globulin, he may erroneously call it a negative test. The amount of globulin seems to bear a certain relation to the cell count and temperature, and follows them pretty closely (see Curves A, B, C, D, and E of Chart X). Comparing five cases of tuberculous meningitis, in which the globulin content was measured by volume each time a spinal puncture was done (every forty-eight hours in each case) and an average cell count made of the fluid, one notes a close relationship. It was not until the fourth case was studied that a difference was noted between the first part of the spinal fluid and the last part withdrawn at the same puncture. Undoubtedly, if averages had been taken in all the

five cases, the curve of the globulin content would follow the curve of the cell count precisely. In all the cases the cell count was the highest at the last puncture, likewise the amount of globulin was greatest. In nearly every case both dropped at just about the time when the temperature made its final drop. There seemed to be no constant relation between the number of cells in the spinal fluid and the amount of globulin in different cases; that is, one case may have a count of 150 cells per cubic millimeter and have 10 per cent. of precipitated globulin by volume, while another case may have fewer cells per cubic millimeter and have almost 50 per cent. of precipitated globulin by volume, both cases being examined the same number of days before the end. The epidemic form of meningitis may have a cell count of 5,000 cells per cubic millimeter with only 20 to 30 per cent. of precipitated globulin by volume. The amount of globulin does not seem to bear any relation to the age. As regards the percentage of globulin, it seemed fairly constant in every case but the last, that of a child of 8 months, which showed almost three times as much as the other cases, in each of which the patient was older. The curves A and C of Chart X are almost identical, the children being of nearly the same age. It is impossible to make any generalizations from only five cases, and one can merely hint at the conclusions which they seem to present. Four out of the five cases had white blood counts below 16,400, and the one with the highest amount of globulin had a white count of 26,000.

The first part of the spinal fluid withdrawn from the spinal canal in cases of tuberculous meningitis differs materially from the last part taken at the same puncture. There is a marked difference in the number of cells, as will be seen in the following cell counts. These figures are the average of five different counts.

| First 10 c.c. Drawn | Last 10 c.c. Drawn |
|---------------------|---------------------|
| 183 cells per c.mm. | 100 cells per c.mm. |
| 190 cells per c.mm. | 120 cells per c.mm. |
| 133 cells per c.mm. | 76 cells per c.mm. |
| 124 cells per c.mm. | 88 cells per c.mm. |
| 206 cells per c.mm. | 160 cells per c.mm. |

The excess of cells in the first part cannot be due to gravity, the child lying usually with its head higher than its pelvis, because other constituents of the spinal fluid, which are in solution, differ accordingly. In some instances there was nearly twice as much globulin in the first part as there was in the last. In the patient 8 months old there was 0.9 c.c. of precipitated globulin in 2 c.c. of the first part of the spinal fluid withdrawn at one of the last punctures, and 0.7 c.c. of precipitated globulin in 2 c.c. of the last part withdrawn at the same puncture. One

of the earlier punctures in the same case showed 0.66 c.c. precipitated globulin in the first part and 0.36 c.c. in the last part. This difference was constant in five lumbar punctures made in each of two different cases. This, again, is too small a number of tests on which to base any conclusions, yet the constancy in all the determinations would make it worthy of further consideration. Should this difference hold good in all cases of meningitis, in which there is a definite inflammation of the meninges, it would be interesting to know whether or not it holds good in other abnormal conditions in which there is a lymphocytic cell count in the spinal fluid, for instance, poliomyelencephalitis, in which the chief lesions are in the spinal cord. Assuming that it does not hold in infantile paralysis, it seems that it ought to be of value in the differential diagnosis between an early infantile paralysis and an early tuberculous meningitis.

Blood.—The lowest white blood count in the whole series was 8,500, while the highest was 48,000. The largest percentage (26.2) showed a leukocyte count between 10,000 and 15,000. There was no relation between the white blood count and the age or stage of the disease, although in the individual cases, in which more than one count was made during the progress of the case, the second count was usually lower than the first. Of the cases which showed a perfectly definite positive von Pirquet reaction, 66 per cent. had an average white count of 13,000, which is somewhat below the average count. Twenty differential counts are given in the accompanying table.

| DIFFERENTIAL COUNT IN TWENTY CASES | | | | | |
|------------------------------------|-----------------|--------------------------------------|--------------------------------|---------------------------------|-------------------------------|
| No. | W. B. C. No. | Polymor- phonuclears Per Cent. | Mononu- clears Per Cent. | Tran- sitionals Per Cent. | Eosino- phils Per Cent. |
| 1 | 26,800 | 74 | 25 | 1 | 0 |
| 2 | 16,400 | 41 | 59 | 0 | 0 |
| 3 | 14,000 | 65 | 33 | 1 | 1 |
| 4 | 9,800 | 55 | 44 | 1 | 0 |
| 5 | 33,600 | 90 | 10 | 0 | 0 |
| 6 | 10,500 | 72 | 28 | 0 | 0 |
| 7 | 9,500 | 79 | 21 | 0 | 0 |
| 8 | 25,000 | 57 | 38 | 4.5 | 0.5 |
| 9 | 22,400 | 90 | 10 | 0 | 0 |
| 10 | 13,200 | 80 | 20 | 0 | 0 |
| 11 | 25,700 | 85 | 15 | 0 | 0 |
| 12 | 15,600 | 80 | 20 | 0 | 0 |
| 13 | 11,000 | 68 | 32 | 0 | 0 |
| 14 | 21,000 | 84 | 16 | 0 | 0 |
| 15 | 26,300 | 80 | 19 | 0 | 1 |
| 16 | 15,400 | 54 | 45 | 0 | 1 |
| 17 | 30,800 | 75 | 25 | 0 | 0 |
| 18 | 36,000 | 74 | 26 | 0 | 0 |
| 19 | 14,000 | 69 | 31 | 0 | 0 |
| 20 | 41,700 | 90 | 10 | 0 | 0 |

The fact that in these twenty cases the eosinophils were practically absent, and also that these patients died, bears out the contention of

Swan and Karsner⁶ that the disappearance of the eosinophils from the circulating blood may be regarded as an unfavorable prognostic sign. It is unfortunately impossible to give the differential counts of cases that have recovered from this almost invariably fatal disease.

Von Pirquet Reaction.—Of the cases in which a von Pirquet test was done, 63 per cent. gave a positive reaction, 25 per cent. a negative reaction, and 2 per cent. are recorded as suggestive. There was no relation between this reaction and the sex. All but three of the patients who were positive to tuberculin had had some previous illness, 35 per cent. having had measles, and 10 per cent. chicken-pox. All but five had comparatively high white blood counts. The relatively high number of positive tests obtained, and the exceedingly high number obtained by Holt and other observers, seem to be contrary to the established teaching that miliary tuberculosis, of which tuberculous meningitis is an example, is "often negative when the tuberculosis is of the miliary type."⁷ Quite frequently, if the first test is negative, a second or third may prove positive. On one particular patient several tests were made on different parts of the body, and at different times, to see at what stage of the disease the body lost its reaction to tuberculin. The reactions on one side of the body were much more intense than on the other, and a test made seventy-two hours before death proved positive in twenty-four hours. Tests with bovine tuberculin were not done. There was no relation between a positive test and the age, for babies of 10 months responded just as frequently as children of 10 years. Nor was there any relation between a positive test and the length of time sick, for positive reactions were obtained all the way from three to fifteen days before the end. The state of unconsciousness did not seem to influence the test, for in over 35 per cent. of the positive cases the patients were unconscious on admittance.

History of Direct Exposure.—There was a definite history of a direct exposure to tuberculosis in 25 per cent. of the cases, no known exposure in 73 per cent., and not recorded in 2 per cent. Of the patients directly exposed, 46 per cent. had had no previous illness, 23 per cent. had had measles, 15 per cent. had had pneumonia and 15 per cent. had had chicken-pox. It seems that this percentage of exposure is indeed smaller than it should be, for if one is energetic enough, he can, in at least 50 per cent. of the cases, elicit some information which will throw light on some tuberculous focus in the family.

Conditions of Lungs on Entrance.—In 30 per cent. of the cases there were sufficient signs in the lungs to show that they were involved

6. Swan, J. M., and Karsner, H. T.: On the Behavior of the Eosinophilic Leukocytes in Cases of Pulmonary Tuberculosis, *New York Med. Jour.*, 1907, lxxxv, 539.

7. Morse, J. L.: *Case Histories in Pediatrics*, 1911, p. 120.

in the tuberculous process. In 70 per cent. the lungs were negative. In two cases d'Espine's sign was recorded as present. In no case was there any record of any palpable mesenteric lymph-nodes. There was a slight general lymph nodular enlargement in many of the cases but it was not constant. A slight cough was present in 30 per cent. of the cases, absent in 57 per cent. and not recorded in 13 per cent. It was present in the last seven of the series, and probably is present in a greater percentage than reported, but the cough is often so slight that parents overlook it, and very frequently it is not asked about in the history taking.

Reflexes.—*Eyes:* In 71 per cent. of the cases the eye reflexes were abnormal, and in 29 per cent. the pupils were equal and reacted normally to light. In 26 per cent. the pupils were equal and reacted sluggishly; in 12 per cent. the pupils were equal but did not react to light; in 4 per cent. the pupils were irregular with no reaction to light; in 1 per cent. they were dilated and irregular, with no reaction to light; in 12 per cent. they were irregular but reacted sluggishly; in 7 per cent. they were dilated and reacted sluggishly; in 4 per cent. they were equally dilated with no reaction to light; in 5 per cent. the condition of the eyes was not mentioned. There was no definite time previous to the end when the eyes lost their reaction to light for as many as twelve to fifteen days before the end of the disease the eyes showed some irregularity, either in size or amount of reaction. Of those patients admitted twenty-four hours before the end nearly all showed an absence of pupillary reaction; all but three of those admitted forty-eight hours before the end showed marked irregularity, extreme sluggishness or no reaction; three were recorded as "equal and normal." Of those admitted three days before the end (15) the pupils were normal in only one; in 3 out of 9 patients admitted four days before the end the pupils were normal; 2 out of 11 patients showed normal pupils five days before the end; 2 out of 8 cases showed normal pupils six days before the end; 3 out of 8 cases showed normal pupils seven days before the end; 3 out of 6 showed normal pupils eight days before the end; 2 out of 7 had normal pupils nine days before the end; 1 out of 3 had normal pupils ten days before the end; 3 out of 6 showed normal pupils eleven days before the end; 2 out of 2 cases had normal pupils twelve days before the end; 5 out of 6 had normal pupils thirteen days or over before the end. In only a few cases (6) was the absence of the winking reflex noted, and that only in late cases.

Knee-Jerks: In over 30 per cent. of the cases the patellar reflexes were equal and active; in 21 per cent. they were absent; in 5 per cent. they were equal and sluggish; in 6 per cent. they were irregular; in 6 per cent. they were not mentioned; in 32 per cent. they were equal

and normal. There was no relation between the character or presence or absence of these reflexes and the sex or age of the patient. They were absent as long as eighteen days before the end, and were equal and active two days before the end.

Babinski's and Oppenheim's Signs: There was a positive Babinski sign in 21 per cent. of the cases, negative in 55 per cent. and not mentioned in 24 per cent. It is more frequent during the latter stages of the disease. The Oppenheim sign is elicited by rubbing the hand or an object along the internal aspect of the tibia and getting extension of the toes. It was obtained in 50 per cent. of the cases in which it was tried and negative in 50 per cent.

Ankle Clonus and Gordon's Sign: Ankle clonus was almost never present as an admitting symptom, though it was rarely reported as being positive. No mention was made as to whether it was a true or pseudoclonus. The Gordon sign, elicited by compressing all the muscles about the lower third of the tibia and getting extension of all the toes, was not mentioned in any of the admitting examinations, but in the last six cases of the series it was present late in the disease.

Abdominal and Epigastric Reflexes: These were positive in 14 per cent., negative in 17 per cent. and not mentioned in 69 per cent. The loss of these reflexes is also one of the late manifestations, usually occurring from three to four days before the end. In a few cases the abdominal reflex disappeared before the epigastric reflex.

Brudzinski's Neck Sign: This very important sign in meningitis, which Brudzinski⁸ thinks is due to hypertonicity of the muscles of the legs and a physiologic predominance of the extensor muscles of the neck and back over the flexor muscles of the legs, was positive in 40 per cent. of the cases, negative in 35 per cent., and not mentioned in 25 per cent. Most of the cases which came in a week or ten days before the end showed the sign more frequently than those coming in early or late. The sign was more frequently present in children between the ages of 2 and 4 than before 2 years and beyond 4. It was practically absent after 5 years.

Brudzinski's Contralateral Sign: This sign is obtained by passively flexing one leg at the hip and getting an accompanying flexion of the other leg, this being known as the identical reflex; but if the leg is extended instead of being flexed, it is called the reciprocal contralateral reflex. Brudzinski⁹ thinks this sign depends on the tendency to bilateral

8. Brudzinski, J.: Un Signe Nouveau sur les membres inférieurs dans les Méningites chez les enfants. *Arch. de méd. d. enf.*, Par., 1909, xii, 745.

9. Brudzinski, J.: Experimentelle Untersuchungen über den Kontralateralen Reflex, und über das Nackenphänomen an den unteren Extremitäten, *Wien. klin. Wchnschr.*, 1911, xxiv, 1795.

innervation of the muscles, which is more pronounced in infants, and that when the cerebrum is diseased there is a tendency to revert or bring out this bilateral innervation. The sign was reported as being positive in only eight cases, negative in eleven cases, and was evidently not looked for in eighty-six of the cases, as no mention of the sign was made. Inasmuch as this sign is a recognized one and very frequently present in meningitis, it seems that it ought to receive more recognition in the physical examination, and its presence or absence noted. In only two cases was there any note of a reciprocal contralateral being present.

Kernig's Sign: The Kernig sign was present in 27 per cent. of the cases, negative in 71 per cent., and not mentioned in 2 per cent. There was no relation between the patellar reflex and Kernig's sign, for it was present just as often in cases of exaggerated knee-jerks as it was in cases of sluggish knee-jerks.

Tache Cérébrale.—This symptom of cerebral involvement was mentioned several times, but in the majority of cases was not. Even though it does appear in other abnormal cranial conditions, yet its presence is a part of the symptom complex of tuberculous meningitis, and its presence or absence should be noted. The fact that, after stroking the skin, a red line appears is not sufficient evidence of a positive *tache cérébrale*. The line of redness should persist for some little time, and is often from one half to one inch in width.

Other Objective Signs.—Paralysis: 43 per cent. of all the cases showed some kind of paralysis. Ocular paralysis (strabismus), single or double, was the most common, occurring in over 61 per cent.; ptosis of the eye-lids occurred in over 15 per cent.; nystagmus in 13 per cent.; facial paralysis in 4 per cent.; paralysis of the tongue in 2 per cent.; of the arms 2 per cent., and of the legs 1 per cent.

Rigidity and Retraction: In 70 per cent. of the cases there was rigidity of the neck and absent in 25 per cent. On an average, it was present five days before the end, and absent on an average of seven days before the end. In 19 per cent. of the cases the head was retracted; in 75 per cent. it was not. Retraction, like rigidity, is also a late manifestation, occurring, on an average, five days before the end. Only one case was reported in which opisthotonos was observed. A slight amount of head retraction will often be missed as long as the patient is observed when lying on the back. Tenderness on flexion of the head was mentioned in a few cases. In practically all of the late cases there was a definite spasticity of the limbs noted.

Bulging Fontanelle: The oldest patient presenting a bulging fontanelle was 18 months and the youngest was 5 months. Over 41 per

cent. of all the children under 18 months had a bulging fontanelle on entrance. One patient 8 months old and one of 12 months had depressed fontanelles three days before death, the duration of the disease in both cases being seventeen days. In one case (12 months) the fontanelle was level; in five cases the fontanelle was tense. Of all the patients presenting bulging fontanelles on entrance, all but three had had convulsions before entering the hospital. One patient had a bulging fontanelle sixteen days before the end, but had been sick three weeks before entrance. In no case was the posterior fontanelle reported bulging. In no case was it necessary to do a ventricular puncture in order to obtain fluid.

Convulsions.—Thirty-nine per cent. of the series had had convulsions before entrance, and 61 per cent. had not, the oldest child being 6 years while the youngest was 8 months. No child over 6 years had had convulsions. Not a few of the patients between the ages of 6 and 22 months had had no convulsions. One case of muscular twitching was reported. The presence of convulsions is also one of the later manifestations, appearing, on an average, four days before the end, and absent, on an average, seven days before the end. In every case but one which showed a bulging fontanelle there was a history of convulsions. Convulsions while in the hospital were rare.

Unconsciousness.—Forty-five per cent. of the patients were unconscious on admittance, and most of those (72 per cent.) were 3 years old or under. There seemed to be no relation between the stage of unconsciousness and the duration of the disease. Four patients admitted on the last day of the disease were unconscious; 10 patients two days before the end were unconscious; 4 patients three days before; 6 patients four days before; 5 patients five days before; 4 patients six days before; 2 patients seven days before; 1 patient eight days before; 4 patients nine days before; 2 patients ten days before. Of those unconscious, in over 80 per cent. there were obtained 20 c.c. or over of spinal fluid, while in 20 per cent. there was less than this amount obtained. The average white blood count of those unconscious was 18,000. Many of those unconscious had comparatively low white counts on entrance. The cell count of the spinal fluid in over 27 per cent. of those unconscious was below 100, while the others ranged between 100 and 300 cells per cm.

Subjective Symptoms.—In practically every history drowsiness, apathy, dulness mentally, languor, irritability and sleepiness were mentioned. In over 85 per cent. vomiting was recorded as an initial symptom, though it seemed to be more frequent at the beginning and the end of the disease rather than in the middle. In 10 per cent. there

was no vomiting. This vomiting, which is of central origin, had no relation to food and seemed to occur at any time of the day. In no case was there any record of projectile vomiting, such as occurs in the meningococcic form of meningitis.

Pain: Pain was a comparatively frequent symptom. The eyes were mentioned as being painful in 1 per cent., the teeth in 1 per cent., the ears in 2 per cent., the neck in 7.5 per cent., the head in 18 per cent., the iliac crests in 1 per cent. and the abdomen in 3 per cent. No pain was recorded in 47.5 per cent. Expressions of pain were evident in 7 per cent. It may be an early or late symptom. Headaches were present in 17 per cent. of the older children.

Other Minor Subjective Symptoms: Fifty per cent. of the cases gave a history of constipation; in 8.5 per cent. the movements were loose; in 23 per cent. they were normal; in 1 per cent. they were irregular. In a few cases picking the nose or eyelids or the bedclothes was noted. Grinding the teeth or gums, restless sleep, delirium, loss of sphincteric control, crying, capricious appetite and inability to swallow were frequently mentioned.

Urine.—In 18 per cent. of the cases acetone was present; a "very slight trace" of albumin was obtained in 7 per cent.; a "slightest possible trace" of albumin in 16.5 per cent. a "slight trace" of albumin in 2 per cent.; a "trace" of albumin in 2 per cent. In 30 per cent. the urine was negative, and in 26 per cent. the urine was not mentioned. Many of the "not mentioned" cases were those of patients who came in moribund and died before a specimen could be obtained. There was no relation between the urinary findings and the sex, white blood count, age or character of the spinal fluid.

Pulse, Temperature and Respiration at the End.—In 41 per cent. there was a final rise of all three curves; in 9 per cent. only a terminal rise of the pulse; in 12.5 per cent. there was a terminal rise of pulse and respiration; in 6.2 per cent. the temperature only rose; in 3.1 per cent. there was a final rise of the temperature and respiration; in 2 per cent. there was an elevation of the respiration, and in 12.5 per cent. there was no final rise of any of the three curves. There was no relation between the terminal rise and the von Pirquet reaction.

Terminal Bronchopneumonia.—From the clinical signs not verified by necropsy, 42 per cent. of the cases were diagnosed as terminal bronchopneumonia, while 61 per cent. of the necropsies done in cases in which death occurred from tuberculous meningitis showed bronchopneumonia to be present. Thirty-seven and five-tenths per cent. of the necropsies showing a terminal bronchopneumonia and 80 per cent. of the necropsies showing no bronchopneumonia were in females, which

would seem to show that a greater percentage of males develop a terminal bronchopneumonia than females. There seemed to be no relation between a terminal pneumonia and the previous illness, or cell count, or the number of lumbar punctures. There was just as large a percentage under 2 years of age who developed a pneumonia as there was under 2 years who did not. The white blood count at entrance was not increased in those cases which later developed a bronchopneumonia.

Relation of Pulse to Temperature.—The character of the pulse depended on the stage of the disease. Patients coming in comparatively early, for instance, two weeks before the end, showed a slow and irregular pulse, while in those in whom the disease was well advanced, the pulse was soft and rapid. Rarely a patient showed a slightly elevated and irregular pulse prior to the stage when it became slow and irregular. In most of the cases the pulse began to rise from one to four days before the temperature. On an average, the pulse began to rise five days before the end, while the temperature, on an average, began to rise two days before the end. A definite remission of symptoms, with a corresponding drop in pulse and temperature, occurred in 64 per cent. of the cases. This fact, as has often been noted, has deceived not a few who are not acquainted with this deceptive phase of the disease. Not infrequently, a patient who has been stuporous and comatose for days will brighten up and actually answer questions from twenty-four to thirty-six hours before death. It is interesting to note that at this stage of the disease there is also a drop in the globulin content and the cell count in the spinal fluid.

No record was kept as to the amount of sugar present in the spinal fluid. In several cases its presence was recorded, while in a few cases a decrease was noted. In no case was it recorded as being entirely absent. The eyes were examined in a few cases, but choroid tubercles were never seen, or if they were, they were never recorded. A moderate conjunctivitis was mentioned in a few cases, which usually came toward the end. No mention was made of any tubercle bacilli having been found in the conjunctival pus. The blood pressure was recorded in only four cases, in each of which it was lower than normal. The reaction of the spinal fluid was mentioned in only a few cases, it being alkaline in every case. The loss of the swallowing reflex occurred as much as ten or eleven days before the end.

Necropsy Findings.—The following list shows the frequency of the various pathologic lesions in eighteen necropsies performed in cases in which death occurred from tuberculous meningitis:

| | | | |
|---|---|---|---|
| Bronchopneumonia | 9 | Miliary tuberculosis of the omentum | 1 |
| Miliary tuberculosis of the lungs ... | 8 | Miliary tuberculosis of the lymph- | |
| Miliary tuberculosis of the pleura... 2 | | nodes | 1 |
| Miliary tuberculosis of the spleen...10 | | Tuberculous ulcerative enteritis..... | 7 |
| Miliary tuberculosis of the liver.... 6 | | Tuberculous ulcerative colitis..... | 2 |
| Miliary tuberculosis of the kidney... 6 | | Old pleuritis | 3 |
| Miliary tuberculosis of the spinal | | Old apical lesions | 3 |
| cord | 3 | Tuberculous ependymitis | 2 |
| Caseous tuberculosis of the liver.... 1 | | Tuberculosis of the kidneys..... | 1 |
| Caseous tuberculosis of the spleen... 1 | | Tuberculosis of the spine..... | 2 |
| Caseous tuberculosis of the lymph- | | Tuberculosis of the appendix..... | 3 |
| nodes | 7 | Tuberculosis of the thymus..... | 2 |
| Caseous tuberculosis of the lungs... 6 | | Tuberculosis of the pleura..... | 1 |
| Enlarged mediastinal lymph-nodes...11 | | Tuberculous dermatitis | 1 |
| Enlarged mesenteric lymph-nodes...10 | | Tuberculous bronchi | 1 |
| Internal hydrocephalus (acute)..... 4 | | Tuberculous ulcerative laryngitis.... 1 | |
| Internal hydrocephalus (chronic).... 1 | | Tuberculous endocarditis | 1 |
| Encephalomalacia | 1 | Tuberculous bronchopneumonia 3 | |
| Miliary tuberculosis of the brain....18 | | Juvenile tuberculous focus of lung... 1 | |
| Solitary tubercle cerebrum | 1 | Localized encephalitis | 1 |
| Solitary tubercle cerebellum | 1 | Rachitis | 2 |
| Solitary tubercle liver..... | 1 | Perisplenitis | 1 |
| Solitary tubercle spleen..... | 1 | Perihepatitis | 1 |
| Tuberculomata cerebellum (mult.)... 1 | | Ulcerative stomatitis | 1 |
| Tuberculomata cerebrum (mult.)... 2 | | Otitis media | 2 |
| Tuberculomata cord (mult.)..... 1 | | Acute fibrous pleurisy..... | 1 |
| Chronic conglom. tubercle lungs.... 6 | | Polyp in duodenum..... | 1 |
| Dilated and hypertrophied heart.... 1 | | Slight cardiac dilatation..... | 1 |
| Subacute gastritis | 2 | Hemorrhagic adrenals | 1 |
| Marked involution of thymus..... 1 | | Cystic ovaries | 1 |
| Colloid struma (incipient)..... | 1 | Bronchitis | 1 |
| Toxic nephropathy | 2 | Acute glomerular nephritis..... | 1 |
| Degenerative myocarditis | 1 | Acute pyelitis | 1 |
| Chronic pachymeningitis external... 1 | | | |

MICROSCOPICAL EXAMINATION

| | | | |
|----------------------------------|---|-------------------------------------|---|
| Kidney (cloudy swelling)..... | 6 | Spleen (folliculous splenitis)..... | 4 |
| Heart (cloudy swelling)..... | 4 | Lungs (emphysema) | 1 |
| Liver (fatty degeneration)..... | 6 | Lungs (atelectasis) | 1 |
| Liver (fatty infiltration) | 4 | Pancreas (cloudy swelling)..... | 1 |
| Liver (cloudy swelling) | 1 | Colon (non-tuberculous ulcer)..... | 1 |
| Spleen (acute hyperplasia)..... | 2 | | |

Mortality.—In no case was there any recovery or remission from the disease. Various measures were tried, among which were large doses of hexamethylenamin and sodium benzoate, and inunctions of mercury. With excessive doses of hexamethylenamin there were no traces of formaldehyd in the spinal fluid.

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ACROCEPHALOSYNDACTYLISM *

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Acrocephalosyndactylism or acrosphenodactylism represents an unusual pathologic or teratologic type which was described at length by Apert¹ in 1906; recently Sterling² has summarized the reports of Apert and his predecessors in a brief review of the nine cases which constitute the basis for the literature of the subject to date. The condition conforms in general to the following description:

The skull is flattened posteriorly in such a manner that the external occipital protuberance is lacking; the squamous portion of the occipital bone is smooth and vertical; just above the lambdoid suture the skull bends forward and upward, reaching its maximum height at the bregma, where it meets, at rather an acute angle, the plane of the forehead and face. Although the frontal area has in general a vertical direction, there is a bulging in the transverse axis of the middle portion, which is separated from the arcus superciliares by a deep furrow. The frontonasal suture is widely open at birth and tends to remain so for the first three or four years of life or longer, while the lambdoid suture is usually solidly closed.

The face is modified more or less. The transzygomatic and trans-temporal diameters are increased. The bridge of the nose is usually depressed and frequently there is exophthalmos. There is a horizontal shelflike projection from the right and left alveolar ridges into the mouth. These projections may even unite in their anterior portions to form a sort of gallery above which is the highly arched hard palate. The teeth are rather irregularly implanted.

In two necropsies on children, aged 2 and 3 months respectively, there was found marked shortening of the base of the skull in the sagittal diameter, involving especially the middle and posterior fossae. The sagittal suture was open from the lesser fontanelle to the root of the nose, being especially wide—about an inch and a quarter—in the frontonasal portion. Wormian bones were present in the posterior fontanelle. The frontal and parietal bones in both specimens presented numerous pits or elliptical depressions on their inner surfaces, where

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1. Apert, E.: *Bull. et mém. Soc. d. hôp. de Paris*, 1906, xxiii, 1310.

2. Sterling: *Ztschr. f. d. ges. Neurol. u. Psychiat. (Referate u. Ergebnisse.)*, 1914, ix, 38.

the bone was extremely thin, and in a few places bony deposit over such areas was absent entirely. During life the bones of the vault of the skull could be indented with the finger. The base of the brain was similarly shortened in its anteroposterior diameter. The occipital lobes were quite small, so that the cerebellum was almost entirely uncovered and the whole organ appeared as though compressed, though no important convolutions were missing. There was no excess of cerebrospinal fluid.³

The hands and feet present a more or less complete syndactylism, which is always of the same type. In the hands the union is more intimate at the tips of the fingers than at the bases, and the hands,



Figs. 1 and 2.—Patient with acrocephalosyndactylism, front and side views of head and face.

therefore, are usually immobilized in the so-called *main d'accoucheur* position. Commonly the nails of the three middle fingers are fused. The thumb as well as the little finger may be free.

The toes are grown together into a homogeneous mass whose anterior edge is bordered by the nails of the fused toes. Frequently the great toe may remain free. In some cases the number of fingers or toes is reduced to four; in others the number may be increased to six or seven, even up to nine.

The etiology of acrocephalosyndactylism is unknown. There is nothing of a familial or hereditary character in connection with the condition. In some cases lues appears in the history; in others hydramnios

3. Wheaton: Tr. Path. Soc. London, 1894, xlv, 238.

was noted during pregnancy, but neither is of constant occurrence. The deformity of the skull is probably the result of the early closure of the sutures at the base and posteriorly. The syndactylism may be due to



Fig. 3.—Syndactylous hands of patient.



Fig. 4.—Feet of patient, showing fusion of toes.

amniotic adhesions, as suggested by Wheaton;³ it has been suggested that there may be a trophic correlation between the faulty development of the base of the brain and that of the extremities. The condition does not necessarily shorten life, and the intelligence of the patient may not

be seriously impaired. The age of the oldest patient described was 21 years. The youngest patients were infants of a few months. No Roentgen ray studies have been reported.

REPORT OF CASE

The present case is that of a girl, $3\frac{1}{2}$ years of age, who was received in the surgical service at the Presbyterian Hospital in November, 1914. She was brought to the hospital for advice concerning deformities of the head, hands and feet, which had been present since birth. Briefly, the history is as follows:



Fig. 5.—Roentgenogram of hands.

The child was born at term, normally, without instrumentation. She was a healthy, breast-fed child until the age of 3 weeks, when she was taken to the North Chicago Hospital for the first of a series of four operations on her hands. Under the influence of the operations and intervening attacks of bronchitis, after the first operation, chicken-pox after the second, measles after the third and whooping cough after the fourth, she remained a puny child until the middle of her second year, since which time she has been in good health and has developed rapidly. She walked at the age of 2 years and 2 months. The patient plays with the other children and the mother maintains that she is as active mentally as they. The father and mother are living and well. There are in the family three other children, aged 15, 13 and 5 years, respectively, who are said to be healthy. The mother had two miscarriages between the second and

fifth pregnancies. No Wassermann tests were made on members of the family other than the patient, in whom the test, using blood serum, was negative. The patient does not appear to be so bright mentally as the mother says she is. She seems to understand what is said to her but she never attempts to form sentences and very rarely attempts a word.

Physical and laboratory examinations disclosed no abnormalities excepting those in the head and extremities, to which exclusive attention may now be given. In general the head is relatively short in the sagittal diameters, and greatly lengthened in the frontomental, bitemporal and bizygomatic diameters. The shape is roughly that of a four-sided pyramid; the apex in the neighborhood of the lambda is rather bluntly rounded, dome-like; the base is represented by the face, which is somewhat diamond shaped, the angles being at the chin,



Fig. 6.—Roentgenogram of feet.

middle of zygomatic arches and the most prominent point on the smoothly rounded, rather bulging, open frontal suture. The face is flat and broad; the forehead high and precipitous, gently rounding laterally into temporal areas which slope outward and downward toward the prominent zygomatic arches. The superciliary ridges are highly arched and flattened. The roof of the orbit may be palpated for about 2 cm. posteriorly from its anterior border. There is marked proptosis; the eyeballs appear to be placed low in the orbits because of the excessive arch and flattening of the supra-orbital ridges. The bridge of the nose is low, but the end bulges out quite markedly. The lips and tongue are normal. There are ten fairly well formed but somewhat irregularly placed teeth in each jaw. The canines are not excessively prominent. The hard palate is of an extremely high arch, the sides coming together at an angle rather than an arch at the highest point, which is located very close to the junction with the soft palate. There is a horizontal shelf-like projection extending nearly the entire length of the alveolar margin of the superior maxilla. The general

shape and relations of this shelf may be ascertained by inspection of Figure 8, in which the condition is somewhat exaggerated. The hair of the head is abundant and of normal texture. The external ears are of normal shape and size.

Examination of roentgenograms of the skull disclosed the following points of interest:

The lambdoid and coronal sutures are closed. The sagittal suture between the nasion and anterior fontanelle is enormously dilated; posterior to the fontanelle it is closed. The sella turcica is markedly deepened and broadened. The orbits are considerably foreshortened and the roof of the orbit arches downward and backward quite sharply. Digital impressions are quite marked in the occipital and posterior portions of the parietal bones. These probably correspond to the pits or elliptical depressions described by Wheaton in his necropsy specimens.

The report of the ophthalmologist (Dr. Darling) on the condition of the eye-grounds is as follows:

Media clear; nerve head gray and margin of disk blurred; could not measure, but looks as if there were some swelling of disk (edema); retinal vessels slightly tortuous.

The following measurements of the head were made:

Diameters—

| | |
|-------------------------------|----------|
| Fronto-occipital | 15.0 cm. |
| Bitemporal | 12.5 cm. |
| Biparietal | 14.5 cm. |
| Frontomental | 17.5 cm. |
| Bizygomatic | 13.5 cm. |
| Transorbital | 10.0 cm. |
| Height of orbits..... | 4.0 cm. |
| Length of frontal suture..... | 9.0 cm. |
| Width of frontal suture..... | 4.0 cm. |

Circumferences—

| | |
|--|----------|
| Fronto-occipital | 48.0 cm. |
| Occipitomental | 51.0 cm. |
| Through gonion of each side and middle of cranium.. | 25.0 cm. |
| Frontomental | 48.0 cm. |
| Through lambda and supraorbital ridges..... | 47.5 cm. |
| From lambda to glabella..... | 28.0 cm. |
| Glabella to bregma..... | 9.0 cm. |
| Auricular point directly across to auricular point of opposite side..... | 34.0 cm. |

The total length of the child was 84 cm.

The present condition of the hands is well shown in Figures 3 and 5. There is irregular fusion of the digits with some angular deformities, apparently due to cicatricial contractures. Practically all the joints in the fingers are stiff. Previous to the series of operations performed during the first year of life, all the digits of each hand were fused in the typical *main d'accoucheur* position. (Personal communication from Dr. Carl Beck who was the surgeon in charge at that time.) The fusion was so complete that but little knowledge could be gained as to the proper lines of cleavage between the phalanges. The separation was thus attempted, rather blindly, of necessity. The work was done with scissors. Roentgenograms made for the present study show conditions to be as follows:

Right Hand.—There are five metacarpal bones; the fourth and fifth are fused for their proximal two-thirds. The proper number of digits is present.

In the thumb there is only one shadow and no suggestion of division or joints. In the index finger there are three phalanges. The terminal phalanx is sharply flexed on the second, and appears to be ventrally curved like a hook. This hook may represent the missing phalanx from the thumb. The proximal interphalangeal joint is replaced by bone. The bones of the middle and ring fingers are closely apposed and seem to be continuous at the level of the proximal interphalangeal joints, while the joints are replaced by bone. The little finger is bent laterally at an obtuse angle, the apex of which is at the first interphalangeal joint; this joint has also been replaced by bone. The character of the joint changes suggests that they are the result of postnatal, inflammatory processes, rather than congenital anomalies.

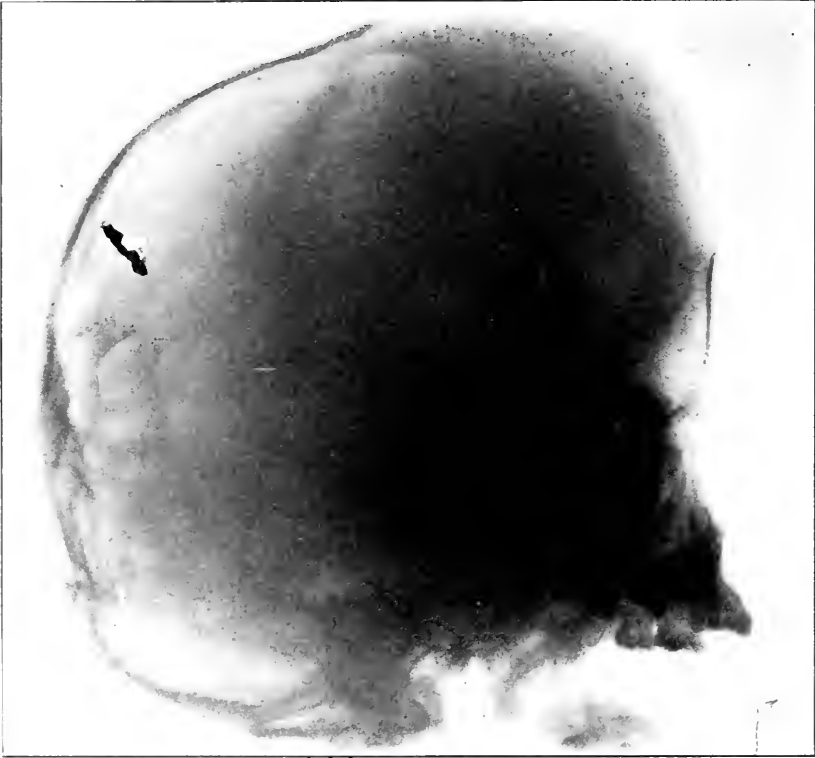


Fig. 7.—Roentgenogram of skull.

Left Hand.—There are five metacarpal bones. The fourth and fifth are fused proximally for one-half their length. There are no bone shadows in the thumb. The three middle fingers present bone shadows suggestive of a phalangeal complement for four fingers. This probably accounts for the bones missing from the thumb. These bones are irregularly fused into a bony plate with, apparently, obliteration of the proximal interphalangeal joints. In the little finger there are shadows of but two bones. There is a gap at the position which the middle phalanx should occupy.

The feet present no abnormalities until the metatarsophalangeal articulations are reached. At this point the webs and interphalangeal spaces fail to appear. Instead there is a uniform extension of the skin of the dorsum to within about

5 mm. of the anterior end of the foot, where it is crossed by a transverse row of nails, shorter and broader than normal, and contiguous with each other. There are five on the left foot and four on the right. On the plantar surface there is a shallow furrow running transversely across the foot just anteriorly to the metatarsophalangeal articulation; it extends dorsally over the medial margin of the foot in the position corresponding to the first phalanx of the great toe. The nail of the great toe of each foot faces laterally and slightly upward. The fleshy plantar pad faces medially and somewhat plantarward. The anterior margin of each foot slopes in a gradual convex curve backward from the medial to the lateral edge; it is slightly serrated, the number of serrations corresponding to the number of nails with one of which each serration is surmounted.



Fig. 8.—Sketch, indicating the deformity of palate.

The phalangeal portion is concave dorsally, convex plantarward; the dorsal concavity (and plantar convexity) is of low grade from the lateral edge medianward until the region of the junction of the first and second digits where there is a rather abrupt dorsal slant due to the marked rotation of the great toe on its long axis. This deformity prevents the patient from wearing shoes unless a large window is cut out over the great toe. There is no web between the digits; they are in close apposition and except at the ends, as mentioned, there is little indication of their presence. There is no independent motion of the portions corresponding to the individual digits, although the digital region as a whole possesses moderate mobility, especially on the little toe side.

Description of roentgenograms of the feet:

In both feet the tarsal bones are normal.

In the right foot there appear to be six metatarsal bones; the first and second are fused distally. The first is incomplete proximally, while distally

it appears to extend without division or other trace of phalanges into the great toe. The fourth and fifth metatarsals are fused in their distal third. Phalangeal rudiments for six toes are present, including in the count the above mentioned distal portion of the first metatarsal.

The left foot is similar to the right except that the union between the first and second metatarsals is considerably more intimate, and the first metatarsal does not extend beyond the line of the metatarsophalangeal articulations. In addition the first and second phalangeal rudiments are closely united throughout their entire length and there is no fusion between metatarsals other than the first two.

Acrocephalosyndactylism seems to be a definite clinical entity presenting characteristic features which are the result of definite pathologic influences at work during intra-uterine life. The demonstration of the nature of these influences is not possible at present.

I am indebted to Dr. Peter Bassoe for the suggestion of the correct diagnosis in the case described above.

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CONGENITAL INTESTINAL OBSTRUCTION *

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Congenital mechanical obstruction of the bowels not due to a developmental defect is so rare a condition that the following case seems worth reporting.

Baby, male, 4 days old, first child, normal delivery, no bowel movement since birth. There had been no stain of meconium on the diapers, which had been observed carefully. Micturition was normal. On the second day the baby vomited a small amount of dark yellow material, rather suggestive of meconium. A second vomiting occurred on the third day, but not on the fourth, although the baby had nursed at four-hour intervals during the day. On the fourth day the abdomen was quite markedly distended and tense, so that no mass could be felt, although there seemed to be rather more resistance on the right side. There was slight dullness in the flanks, especially the right. Visible peristalsis was distinct and continuous. There was no intermittent crying suggestive of intussusception. A finger could be inserted 2 inches or more into the rectum and nothing could be felt except that the rectum seemed somewhat tighter than usual. Repeated soapsuds enemas brought no stain of meconium or blood—only very scanty mucus. Not over one ounce actually entered the bowel, the return flow pouring out around the catheter. At 2 p. m. on the fourth day the temperature was 102; at 8 p. m. it was 100.5. The child's color was good and its general condition good. The head was kept well retracted with moderate spasm. The chest was normal.

The child was taken to the hospital and the abdomen opened at 10 p. m. (fourth day). Immediately clear, slightly yellowish serous fluid poured out. On evisceration the condition was readily seen to be a complete twist of the mesentery of the small intestine with complete obstruction approximately at the middle of the small intestine. On untwisting, gas escaped through into the collapsed bowel beyond. The appendix, sharply coiled, and the ileocecal region were normal. The abdomen was closed and the child seemed to be in good condition. A catheter inserted into the rectum allowed a small amount of gas to escape but nothing else. During the night there were two good bowel movements of meconium. The next day the child seemed to be in fair condition in spite of a temperature of 104. There was a series of about ten bowel movements. Toward evening the color of the ears and the fingers became livid. The temperature, pulse and respiration continued high, the latter about 100. The head was retracted, the legs relaxed. The forehead was kept tonically wrinkled and the eyes wide open, suggestive of an abdominal facies, although the abdomen was soft and not unduly distended. The child died about thirty hours after the operation. Necropsy was not permitted.

When one is confronted with a case of intestinal obstruction at birth, the presumptive diagnosis is some developmental defect, the most common being intestinal atresia. The foregoing case is one of the rare instances in which a more remediable condition existed and is

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instructive from the point of view of prognosis and treatment of these cases as a class. A fairly careful review of the literature shows only four cases at all comparable to the one reported. These are referred to again in an excellent article by N. I. Spriggs,¹ perhaps the most comprehensive recent publication on the subject in English. A very complete bibliography is appended. The first of these cases was reported by Harrison Cripps in 1880, a case of congenital volvulus of the lower ileum. On rectal examination it was noted the little finger could be introduced a fair distance, but seemed to meet an obstruction suggesting a blind end. A congenital atresia was diagnosed and an inguinal enterostomy performed on the third day. There had been persistent vomiting and complete obstruction. The child died from peritonitis. At the necropsy the rectum, colon and about 2 feet of the ileum were found intact but extremely small, having about the caliber of a pipe-stem. A loop of ileum at this point was completely twisted on itself with distended bowel above. The undeveloped lower bowel was explained to be due to the absence of meconium from early fetal life and the consequent lack of stimulation to growth.

Newton Pitt in 1891 reported a similar case of congenital volvulus of the ileum, 2 feet from the ileocecal valve. It was also regarded as a case of imperforate rectum and inguinal colostomy performed. At necropsy a sharp line of demarcation could be seen between the strangulated and healthy bowel.

Spriggs also refers to Carwardine's case of congenital volvulus occurring at the point of Meckel's diverticulum with completely collapsed bowel below, and to another case by Eschback. None of these, however, had a complete twist of the mesentery as in the case reported above.

These cases, rightly considered, merely represent a more hopeful group of the general class of congenital intestinal obstruction. They may only differ in degree from the rest, since fetal volvulus, like other fetal accidents, such as intussusception, kinking, peritonitis, etc., have been pretty well shown to play a part in the causation of intestinal atresia. The etiology of the latter condition seems to be a very complex one. A large proportion of intestinal atresias occur at the location of some embryologic event such as the junction of the vitelline duct with the bowel or of the common bile-duct, which really indicates the point of the original evagination to form the liver, or the point of fusion between the hindgut with the proctodeum. There are many instances of atresia at other points, however. In fact, atresia of the alimentary tract may occur at any point or, although less frequent, at multiple points between the pharynx and anus. For this reason and

1. Spriggs, N. I.: Congenital Occlusion, *Guy's Hosp. Rep.*, 1912, lxvi, 143.

from embryologic evidence, Kreuter and others hold to the theory that atresias are the result of the suspension of the process of canalization of the solid intestinal cord which exists in the early fetal life of vertebrates. Again, vascular accidents may be instrumental in this lack of development.

The symptoms of obstruction of the bowels at birth seem to be identical whether there is atresia or mechanical obstruction without atresia. Constipation usually is absolute from birth, because the condition usually dates from early fetal life before meconium has reached the lower bowel. There are a few cases on record, however, in which a few movements occurred just after birth and then stopped. In some a prenatal obstruction was obvious at necropsy. On attempting to give enemas it is frequently reported that the injection fluid returns directly around the catheter or at most 1 or 2 ounces are retained. This, together with the absence of any meconium or blood stains, has repeatedly led to the error of diagnosing a rectal atresia, which may be seemingly confirmed by an apparent obstruction of the rectum on digital examination. Perineal operations have been attempted under these conditions and valuable time lost without relieving the obstruction. If there is an imperforate rectum only, a bulging distended bowel should be palpated, especially when the child cries. If collapsed or small undeveloped bowel is encountered, there is probably atresia much farther up in the abdomen. In the first place, it should be remembered that rectal atresia practically always occurs within two inches of the anus.

As in acquired ileus, vomiting is a practically constant symptom and occurs early, usually the second day. The vomitus may contain meconium, bile or blood-stained mucus, the character of it giving some clue to the level of the obstruction. The child may nurse fairly well.

Distention nearly always occurs, but is not usually present at birth, although in a case reported by MacCallum it was so extreme as to interfere with parturition. This was due, however, to fetal peritonitis with many adhesions.

Icterus neonatorum has been mentioned as a symptom, but it would be difficult to say whether it is more frequent in these cases than in normal new-born infants. Visible peristalsis is of considerable aid especially when the obstruction is high and associated with gastric dilatation, which might be determined by percussion, skiagraphy or lavage. Free peritoneal fluid should also be examined for. Anuria has been described, even in cases in which there were no developmental defects in the urinary system. Convulsions have also occurred.

In the diagnosis it might bear repeating that too much attention should not be paid to a questionable stenosis of the rectum 2 inches or

more from the anus, because the lower bowel may be extremely small and undeveloped from a high obstruction. The possibility of general peritonitis must also be considered.

The prognosis in these cases is somewhat different from that of intestinal obstruction in adults. Serious symptoms develop comparatively less rapidly. The majority of patients will die in the first week, although many are on record living from fifteen to eighteen days. In general, the lower the obstruction the longer they will live. Cripps reported a case of imperforate rectum in which operation was refused on the third day. The child was brought back at the end of a month with little change in its condition in spite of fecal vomiting every two days. Spriggs quotes a case of a girl of 14 years with complete rectal occlusion, who vomited her feces every few days. A well-marked stenosis may cause little or no symptoms, but is probably the cause of some cases of Hirschsprung's disease later in life. It should be remembered that inspissated meconium may cause complete obstruction which may be fatal, or may be spontaneously relieved. There is a case on record² in which a child with congenital obstruction was in such desperate condition on the third day that operation seemed inadvisable. When it was 5½ days old, during a spell of crying, a mass of meconium was expelled, followed by a series of copious movements. The child fully recovered. For this reason it would seem justifiable to give gentle massage and enemias a fair test—for a short period of time, however, since the loss in weight is so rapid and the operative risk at best great. Spriggs states that in at least eighty-two cases of operation there has not been a single recovery, although two patients lived a couple of weeks. Most of the cases, however, had extensive anastomoses or enterostomies. The practical point is that conditions such as volvulus, intussusception, etc., at or before birth cannot be distinguished from intestinal atresia, which is hopeless without operation and operation for the former conditions might succeed in a fair proportion of cases.

2. *Med. Rec.*, 1899, lvi, 133

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THE USE OF BISMUTH PILLS IN THE FLUOROSCOPIC EXAMINATION OF THE INFANT'S STOMACH *

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The use of pills for gastric tests suggested itself in the course of the employment of the duodenal catheter for ascertaining the size of the pylorus in infants. The size of the catheter which can be readily introduced past the pylorus in the newborn as well as in somewhat older infants¹—the approximate circumferences of the pylorus at these periods of life—having been ascertained, it seemed that the same infor-



Fig. 1.—Two-months-old baby. After one hour both pills are within stomach.

mation could be obtained more easily through the use of pills having definite circumferences. Accordingly, bismuth pills were prepared of three sizes (9, 15 and 21 mm. in circumference), and coated with many layers of keratin to prevent their dissolution by the gastric juice.

The use of pills has certain advantages over that of a powder suspended in milk, which is the usual way of giving bismuth to infants

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1. Hess, A. F.: The Pylorus, Pylorospasm and Allied Spasms, *AM. JOUR. DIS. CHILD.*, 1914, vii, 184.

for radioscopic examination of the stomach. The introduction of the pill is very simple; it is placed on the dorsum of the tongue and pushed down gently into the pharynx by means of the finger. This would seem less harmful than pouring a considerable amount of bismuth mixture into the stomach. It was anticipated that the fluoroscopic picture would be more clearly defined with the use of the pill, and that we would be able to judge with greater certainty whether or not



Fig. 2.—Same case as Figure 1. Large pill out of stomach; small pill in stomach after two hours.



Fig. 3.—Same case as Figures 1 and 2. After three hours both pills out of stomach.

all the bismuth had left the stomach. Experience served to verify this opinion. When a suspension of bismuth is used, judgment is hampered frequently by a portion of the bismuth remaining in the stomach, while another portion has passed into the intestine.

Our first experiences soon convinced us, however, that we could not make use of these pills for the purpose of gauging the diameter of

the normal pylorus, for it was evident that the pills did not leave the stomach and enter the intestine according to their size. It was found that although a small and a large pill were given, for example, 9 F. or 15 F., there might be no difference in the time of their entering the intestine, as determined by fluoroscopic examinations carried out at half hour intervals. Moreover, if one did traverse the pylorus in advance of the other, it was almost always the larger and not the



Fig. 4.—Six-months-old baby. After one hour both pills are within the stomach.



Fig. 5.—Same case as Figure 4. After two hours both pills are within the stomach, near pylorus.

smaller pill. Figures 1, 2 and 3 illustrate this observation. In this case, two pills—No. 9 and No. 15—were given. Roentgenogram 1 was taken one hour later, and shows both pills still within the stomach; Figure 2, taken after two hours, shows the larger pill out of the stomach and the smaller one still within the gastric cavity; Figure 3, taken after a three hour period, portrays both pills out of the stomach.

TABLE 1.—SHOWING TIME OF PASSAGE OF PILLS FROM STOMACH IN CASE 1
Ida C., aged 5½ months; dyspepsia, atrophy; weight, 11¼ pounds.

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Remarks |
|----------|---------------|-------------|---|--|--|--------------------------|
| 10/16/14 | 9, 15 | 1:40 p. m. | 2½ hours 4 hours | Both in stomach Both out of stomach | Out 2½-4 hrs. | |
| 10/20/14 | 9, 15 | 1:10 p. m. | 2½ hours | Both out of stomach | Out within 2½ hrs. | |
| 10/24/14 | 9, 21 | 1:45 p. m. | 2 hours 3 hours 3¾ hours 4 hours | No. 21 out and No. 9 in stomach No. 21 out and No. 9 in stomach No. 21 out and No. 9 in stomach Both out of stomach | No. 21 out in 2 hrs. No. 9 out in 3¼-4 hrs. | Larger pill out earlier. |
| 11/17/14 | 9, 15 | 10:00 a. m. | 1 hour 2 hours 3 hours | Both in stomach No. 15 out and No. 9 in stomach Both out of stomach | No. 15 out in 1 hr. No. 9 out in 2-3 hrs. | Larger pill out earlier. |
| 11/21/14 | 9, 15 | 10:00 a. m. | 1½ hours 2½ hours 3½ hours | Both in stomach Both in stomach Both out of stomach | Out 2½-3½ hrs. | |

Epieriesis: Larger pill left stomach either at same time or earlier than smaller pill.

This result at first was quite surprising; further tests convinced us that it should be regarded as not exceptional, and that in cases manifesting no obstruction of the pylorus, where one pill does leave the stomach before the other, it will almost invariably be the larger one; for example, see Table 1, Case 1.

Frequently pills are noted to have left the stomach at about the same time, irrespective of their size. Figures 4, 5 and 6 show this result in roentgenograms taken one, two, and three hours following the introduction of a No. 9 and a No. 15 pill. The first and second show both pills within the stomach, and the third shows both in the intestine.² It is realized that the second roentgenogram is not convincing in this regard. But it should be borne in mind that this study



Fig. 6.—Same case as Figures 4 and 5. After three hours both pills out of stomach; one disintegrating.

was carried out, not by means of roentgenography, but almost entirely with the aid of the fluoroscope; the diagnosis as to the site of the pills depended on the fluoroscopic picture and not on the roentgenogram. The infants were observed generally at one hour intervals until the pills were noted to have left the stomach. In some cases, notably in a rather severe case of pyloric obstruction, referred to below, these fluoroscopic examinations necessitated frequent tests which had to be prolonged well into the night. It is a pleasure to thank Dr. Brim for

2. In order to ascertain whether our results were influenced mainly by the weight rather than the size of the pills, and whether this factor could account for the larger pill leaving the stomach as quickly or more quickly than the smaller one, we had some lighter pills made, composed of half licorice and half bismuth. Tests showed that these followed the same sequence in entering the intestine. In the summary of tests of Case 4 will be found one in which a lighter and a heavier No. 15 pill were given, and another in which a No. 9 and No. 15 licorice pill were given. In both instances the pills left the stomach within the same interval.

his cordial cooperation in this work, as well as Dr. Charles Gottlieb, who was kind enough to take the roentgenograms which illustrate this article. The fluoroscopic picture is almost always quite clear. The pill is sharply outlined within the infant's stomach, which, as is well known, is characterized by its large air bubble, which develops as a result of the lack of gastric peristole. When the infant is moved from one position to another, the pill rolls along the greater curvature in a corresponding direction. Sometimes it is at first difficult to decide whether it lies within the stomach or within the intestine. In such an event, the infant is turned first on one side and then on the other, and we note whether the pill moves, as should be expected, towards the pylorus, or towards the cardia. The crucial test consists in suspending the child by its feet and examining it in the inverted position. Under



Fig. 7.—Upright posture. Pill at greater curvature; air bubbles and fluid above (exposure dorsoventral).

these conditions if the pill is within the stomach, it will assume a position close beneath the diaphragm, whereas if it is in the intestine, it will be lower down in the abdominal cavity. Figures 7 and 10 clearly demonstrate this point. The former shows the baby held in the normal vertical position and the pill fallen to the greater curvature; the latter shows the baby inverted, the pill having completely changed its position and dropped to the lesser curvature, the diaphragmatic portion of the stomach. In this position, surmounted by a layer of fluid and a large gastric air bubble, there can be no question as to whether the pill is within the stomach or the intestine.

Just as it is possible to alter the position of the pill in a vertical direction, so we can at will divert it laterally to the right or to the left. Figure 8 illustrates an infant lying on its right side and the pill at the pylorus; Figure 9 shows the same infant a few minutes later lying on its left side, and the pill far over along the left border of the

stomach. These pills were poorly made and show some disintegration within the stomach.

It may be stated as a corollary to this postural variation, that, merely by placing an infant on one side or the other, it was possible to hasten or to retard the passage of the pills into the intestine. A striking experiment of this kind is summarized under Case 4 (Table 4). It will be noted that the emptying time of the stomach of this infant was about one to two hours; that by keeping it on its left side (January 26 test), the passage of a small and a larger pill was delayed over four hours; that two days later, when the infant was placed on its right side, both pills had left the stomach within one and a quarter hours.

An opportunity presented itself of making use of this test in several cases of pylorospasm. The first was a typical case; a baby about 2



Fig. 8.—Same as Figure 7 five minutes later. Lying on right side. Pill at pylorus. Air bubble in left portion of stomach (exposure dorsoventral).

months old, breast fed, which had had projectile vomiting almost since birth. In the course of about five weeks some eighteen tests were carried out on this infant, comprising numerous fluoroscopic examinations and in some instances also roentgenograms. Visible peristalsis, obstruction to the duodenal catheter, marked gastric dilatation, and constant evidence of retention were present. The pills in this case were retained in the stomach frequently for about eight hours, and in one instance for over fourteen hours (Fig. 11). It seems unnecessary to consider the details of these several tests; however, the summary of Case 2, Table 2, may be of interest.

It may be well to mention a few points which Case 2 illustrates. In the first place it will be noted that the pills were very frequently macerated; evidently they were subjected to exceptional mechanical pressure within the stomach, incurred probably in the course of various

TABLE 2.—TIME OF PASSAGE OF PILLS FROM STOMACH IN CASE 2
William M., aged 2 months; pylorospasm; breastfed q. four hours.

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Vomiting | Remarks |
|----------|---------------|-------------|--|---|---|--------------------|--|
| 12/19/14 | 9, 15 | 9:45 a. m. | 11:15 a. m. 1:15 p. m. 1:15 | Both in stomach Both in stomach Both out of stomach | Macerated (both) Out 2½-3½ hrs. | Projectile | Stomach large, dis- tended. |
| 12/20/14 | 9, 15 | 9:45 a. m. | 11:00 a. m. 12:00 m. 1:00 p. m. 1:30 | Both in stomach Both in stomach Both in stomach Both out of stomach | Pills macerated Out 3¼-3¾ hrs. | Projectile | |
| 12/22/14 | 15, 21 | 10:00 a. m. | 11:00 a. m. 12:00 m. 12:30 1:15 p. m. 2:00 3:00 3:00 4:00 4:45 5:15 6:15 7:00 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Out 8¼-9 hrs. | Projectile | |
| 12/24/14 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:00 p. m. 2:00 4:00 5:30 6:30 7:30 8:45 | Both in stomach Both in stomach Both in stomach, fed Both in stomach Both in stomach Both in stomach, fed Both in stomach Both out of stomach | Out 9½-10¼ hrs. | Projectile | |
| 12/27/14 | 9, 15 | 9:45 a. m. | 11:15 a. m. 12:15 1:15 p. m. 2:25 3:30 4:30 5:15 | No. 9 out and No. 15 in stomach No. 9 out and No. 15 in stomach No. 9 out and No. 15 in stomach No. 9 out and No. 15 in stomach No. 9 out and No. 15 in stomach Both out of stomach | No. 9 out within 1½ hrs. No. 15 out between 6¾-7½ hrs. | Projectile | Papaverin, three doses (0.01 gm.). Fed at 2 p. m. |
| 12/28/14 | 9, 15 | 1:00 p. m. | 2:15 3:15 4:20 5:20 6:30 8:00 9:30 10:40 11:50 12:50 m. 1:30 a. m. 2:15 3:15 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Out 13¼-14¼ hrs. | Projectile Less | Papaverin, five doses (0.01 gm.). Fed q. four hours. |

| | | | | | | |
|----------|-----------------------------|---|--|---------------------------------------|----------------------|--|
| 12/30/14 | 9, 21 | 9:45 a. m. 11:30 a. m. 12:15 m. 1:15 p. m. 2:30 4:20 5:30 6:30 7:15 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Portions out of stomach All out of stomach | Macerated Out 8¼-9½ hrs. | Very much diminished | Papaverin. |
| 12/31/14 | 15, 21 | 9:45 a. m. 11:00 a. m. 12:15 m. 1:30 p. m. 2:30 3:30 4:30 5:30 6:00 7:15 8:15 8:45 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Part out of stomach Part out of stomach Part out of stomach All out of stomach | Macerated Out 10½-11 hrs. | Less | |
| 1/4/15 | 15, Bismuth 15, Licorice | 9:45 a. m. 11:00 a. m. 12:30 m. 1:30 p. m. 2:30 3:30 4:30 5:30 | Both out of stomach | Out 6¾-7¼ hrs. | Once in last 4 days | Papaverin. |
| 1/5/15 | 9 Licorice 15, Licorice | 9:45 a. m. 11:00 a. m. 12:30 m. 1:30 p. m. 2:30 3:30 4:30 5:30 6:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Out of stomach | Macerated Out 7¾-8¾ hrs. | Less | Papaverin. Bottle and breast feeding. |
| 1/9/15 | 9, 21 | 9:45 a. m. 11:00 a. m. 12:00 m. 1:00 p. m. 2:30 4:00 5:00 6:30 7:30 8:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Macerated Out 9¼-10¾ hrs. | Less | Papaverin. |
| 1/12/15 | 9, 15 | 9:30 a. m. 10:30 a. m. 11:30 1:30 p. m. 2:30 3:30 4:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Out 6-7 hrs. | None | Papaverin. |

TABLE 2.—TIME OF PASSAGE OF PILLS FROM STOMACH IN CASE 2—(Continued)

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Vomiting | Remarks |
|---------|---------------|-------------|---|--|------------------------------------|----------|--------------------------------|
| 1 14/15 | 9, 15 | 9:30 a. m. | 10:30 a. m. 11:30 1:00 p. m. 2:30 3:30 4:30 5:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Macerated Out 7 8 hrs. | None | Papaverin. |
| 1 15/15 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:00 p. m. 2:00 2:45 | Both in stomach Both in stomach Both in stomach Both out of stomach | Out 4-4 1/4 hrs. | None | Papaverin. |
| 1 16/15 | 9, 21 | 10:00 a. m. | 11:00 a. m. 12:30 m. 1:30 p. m. 2:30 3:30 4:30 5:30 6:30 7:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Macerated Out 8 1/2-9 1/2 hrs. | Twice | No papaverin. |
| 1 17/15 | 9, 21 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:30 p. m. 2:30 3:30 4:30 5:30 6:30 7:30 8:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | | None | No papaverin. |
| 1 23/15 | 9, 21 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:00 p. m. 2:00 3:00 4:30 5:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Macerated Out 9 1/2-10 1/2 hrs. | None | Adrenalin in IV (1:10,000). |
| 1 26/15 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:30 p. m. 2:30 3:30 4:30 5:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Out 6 1/2-7 1/2 hrs. | | Adrenalin in IV. |

Epietisis: Case of marked pylorospasm. Papaverin diminished the vomiting, although it did not seem to enable pills to enter intestine earlier.

attempts to pass the constricted pylorus. This case may also be of interest as affording repeated opportunity for testing the effect of papaverin on pylorospasm in an infant. This alkaloid is a derivative of opium and has been recommended especially to counteract the spasm of smooth muscle. It was given by us subcutaneously in the dose of 0.01 gm. Although it will be noted in the summary that the papaverin did not facilitate markedly the passage of the pills from the stomach, it had an undoubted effect on the vomiting, which became decidedly less marked under its influence. The papaverin delayed the passage of the pills through the intestine, as might be expected, considering its inhibiting effect on all smooth muscle.

In mild pylorospasm, however, papaverin may effect not only diminution of the vomiting, but hasten the passage of pills, and probably of food, from the stomach into the intestine. This was noted in



Fig. 9.—Same as Figure 8, five minutes later. Lying on left side. Pill at left border of stomach; air bubble extending to pyloric region (exposure dorso-ventral).

two instances. The first concerned a baby that had vomited since birth, and manifested obstruction to the passage of the duodenal catheter and a retention of the pills within the stomach for about seven hours (Case 3). When papaverin was given, both the small and the large pill were seen to have left the stomach after one or two hours. On discontinuing the drug, this period was extended to four to five hours, to be curtailed once more to one to two hours on resuming the medication. This case seemed particularly convincing as evidencing the value of this drug in some cases. Table 3 gives a summary of Case 3.

In the article on pylorospasm mentioned above, reference was made to a type of spasm of the pylorus termed "secondary pylorospasm." By this term an acute spasm of the pylorus is understood, a transitory hypertonic state. This condition is readily overlooked, as it is masked generally by the symptoms of the complicating dyspepsia.

TABLE 3. TIME OF PASSAGE OF PILLS FROM STOMACH IN CASE 3
Sam H., aged 6 months; weight, 10¼ pounds.

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Remarks |
|----------|---------------|-------------|---|---|--|--|
| 11/3/14 | 15, 21 | 2:00 p. m. | 1:45 p. m. 5:55 6:40 7:30 8:20 9:00 9:30 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach Both out of stomach | Out 7-7½ hrs. Both out within 1¼ hrs. | Vomited. Three doses papaverin (0.01 gm.). |
| 11/7/14 | 15, 21 | 10:00 a. m. | 11:15 a. m. | Both out of stomach | Out within 2¼ hrs. | Five doses papaverin. Papaverin discontinued. |
| 11/12/14 | 9, 15 | 1:45 p. m. | 3:55 p. m. | Both out of stomach | Out 4 5¼ hrs. | Three doses papaverin. |
| 11/14/14 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:00 p. m. 2:00 3:15 | Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | Out 1-2¼ hrs. | Three doses papaverin. |
| 11/24/14 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:15 m. | Both in stomach | Out 6-6¾ hrs. | |
| 11/26/14 | 9, 15 | 10:10 a. m. | 11:30 a. m. 12:30 m. 1:30 p. m. 2:30 4:00 4:50 | Both in stomach Both in stomach Both in stomach Both in stomach Both in stomach Both out of stomach | | |

Epicrisis: Case of mild pylorospasm. Infant had projectile vomiting almost since birth. Some obstruction to passage of catheter. Delay in passage of pills from stomach, the interval being shortened by means of papaverin from over seven hours to about two hours. When the drug was discontinued the period was again prolonged (five hours).

A case of this nature was encountered in the fall of 1913 in one of the earliest tests made with the pills. The baby was 2 months old, and it had been possible to pass not only the ordinary duodenal catheter, but even a No. 18 and a No. 20, and the dilatable catheter (Case 5). We had concluded from the many tests made on this infant that its pylorus was especially patent and relaxed. Somewhat later it developed dyspepsia, manifested by marked vomiting. When the pills were



Fig. 10.—Same as Figure 9 five minutes later. Infant inverted in vertical position. Pill at diaphragm; air bubble at greater curvature (exposure dorso-ventral).



Fig. 11.—Case of pylorospasm (2 months old) showing No. 9 and No. 15 pills in stomach after thirteen hours. Notice marked dilatation of stomach and remnants in intestine of pills given on previous days.

introduced at this time, they did not leave the stomach for thirty hours, although in previous tests, the time of entering the intestine had been less than three or four hours. The case is summarized in Table 5.

In this connection we may add that tests by means of the pills have strengthened us in the opinion that in cases of pylorospasm there

TABLE 4. TIME OF EMPTYING STOMACH IN CASE 4
Morris F., aged 7 months.

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Remarks |
|---------|-----------------------------|-------------|---|--|--------------------|--|
| 1/19/15 | 9, 15 | 9:45 a. m. | 11:15 a. m. | Both out of stomach | Out within 1½ hrs. | Aspiration 1½ hours after feeding, showing 60 c.c. fluid in stomach. |
| 1/22/15 | 9, 21 | 10:00 a. m. | 11:00 a. m. 12:30 m. | Both in stomach Both out of stomach | Out 1 2½ hrs. | |
| 1/30/15 | 9, 21 | 9:45 a. m. | 11:30 a. m. | Both out of stomach | Out within 1¾ hrs. | |
| 1/31/15 | 15, 21 | 9:45 a. m. | 11:00 a. m. 12:15 m. 1:00 p. m. | Both in stomach Both in stomach Both out of stomach | Out 2½-3¼ hrs. | Licorice pill used. |
| 1/4/15 | 15 13, Licorice | 9:45 a. m. | 11:00 a. m. 12:00 m. | Both in stomach Both out of stomach | Out 1¾-2¼ hrs. | |
| 1/5/15 | 9, Licorice 15, Licorice | 9:45 a. m. | 11:00 a. m. 12:30 m. | Both in stomach Both out of stomach | Out 1¾-2¼ hrs. | Licorice pills used. |
| 1/22/15 | 9, 15 | 10:00 a. m. | 11:00 a. m. | Both out of stomach | Out within 1 hr. | |
| 1/23/15 | 9, 15 | 10:00 a. m. | 10:30 a. m. 11:00 11:30 | Both in stomach Both in stomach Both out of stomach | Out 1½ hrs. | Adrenalin m. V (1-10,000). Adrenalin m. V (1-10,000). |
| 1/26/15 | 9, 15 | 10:00 a. m. | 11:00 a. m. 12:00 m. 1:30 p. m. 2:30 3:20 | Both in stomach Both in stomach Both in stomach Both out of stomach | Out 4½-5½ hrs. | |
| 1/28/15 | 9, 15 | 10:15 a. m. | 11:30 a. m. | Both out of stomach | Out within 1¼ hrs. | No drug. Kept on left side. |
| | | | | | | No drug. Kept on right side. |

Epiptosis: Case with early emptying of the stomach. Passage into intestine markedly delayed by keeping infant on left side.

is frequently marked relaxation of the pylorus during the late stage of the illness. This phenomenon has already been noted in connection with a consideration of pylorospasm in its relation to duodenal catheterization. It was again clearly manifested by a case in which the pills throughout many tests had been greatly delayed in their passage from the stomach, but where six days previous to death, they were noted to have left the stomach within one to two hours. A sharp reversal of the fluoroscopic picture had taken place. These roentgenographic results harmonize with a similar change as to the passage of the catheter, and strengthen our opinion that pyloric relaxation is commonly a late manifestation of pylorospasm, and that it leads to a rapid passage of food into the intestine and to alimentary intoxication, the ultimate cause of death.

CONCLUSIONS

The foregoing study was carried out by means of keratin coated bismuth pills having definite circumferences corresponding to the size of the catheters, which we have shown can readily be introduced past the pylorus in infants. The purpose was to furnish a simple means of gauging the size of the pylorus and judging whether this sphincter was normally patent or not. It was found that under normal conditions objects do not leave the stomach in direct ratio to their size; that, in fact, larger objects are apt to be propelled into the intestine more quickly than smaller ones. This raises the question whether, following this analogy, food which has been insufficiently masticated may not remain in the stomach for a shorter rather than for a longer period than food that has been more thoroughly comminuted. Probably this is frequently the case. Under these conditions less work would be imposed on the stomach and proportionately more on the intestine, with the danger of consequent intestinal indigestion.

There was a marked difference in the emptying time of the stomach, according to the posture of the infant. The delay in the passage of the pills when the infant lay on its left side, and the hastening of their passage when the infant was placed on its right side, were almost constant phenomena. It would seem that this observation has clinical significance and is capable of practical adaptation. It may prove to be of advantage to place infants on the right side when there is an evident delay in gastric digestion.

In cases of pylorospasm there was a retardation in the passage of the pills from the stomach into the intestine. The degree of this delay varied in accordance with the degree of obstruction. The test does not enable us, however, to make a differential diagnosis as to the func-

TABLE 5.—TIME OF EMPTYING STOMACH IN CASE 5
Anne R., aged 2 months; dyspepsia; weight, 8 pounds.

| Date | Size of Pills | Given at | Fluoroscoped | Site of Pills | Summary | Remarks |
|--------------|---------------|-------------|---|--|--------------------------------------|---|
| 11/30/14 | | | | | | No. 15, No. 18 and No. 20 catheters passed into duodenum. Bile obtained. |
| 11/30/14 | | | | | | Same result as in first test. |
| 12/2/14 | | | | | | No. 15 and No. 18 catheters passed. Bile obtained. More difficult than previously. No. 20 could not pass. Grip—temperature 100. |
| 12/4 & 5/14 | | | | | | No. 15 and No. 18 catheters passed, No. 20 dilatible catheter passed; bile obtained. |
| 12/9 & 11/14 | | | | | | Larger dilatible No. 21 F. catheter passed. |
| 12/21/14 | | | | | | Balloon of catheter dilated to fully 0.5 cm., pulled back through cardia and pylorus. |
| 12/24/14 | 15 | 11:00 a. m. | 3:30 p. m. | Out of stomach | Out within 4½ hrs. | Only one examination made. |
| 12/26/14 | 15 | 11:00 a. m. | 2:00 p. m. | Out of stomach | Out within 3 hrs. | Only one examination made. |
| 12/29/14 | 15 | 12:00 m. | 3 hours 4 hours 5¼ hours 11 hours 24 hours 27¼ hours 29 hours 30 hours 48 hours | In stomach In stomach In stomach In stomach In stomach In stomach In stomach In stomach Out of stomach | In stomach at least 30 hrs. | Tried to pass duodenal catheter fully six times without success. No bile obtained. Grip. Slight vomiting. |

Epericrisis: Case with marked relaxation of pylorus, as shown by the rapid passage of pills and frequent passage of catheters of large diameter. Secondary pylorospasm manifested by failure to pass catheter and long delay in the passage of pill into the intestine.

tional or the organic nature of the obstruction. In cases characterized by pyloric obstruction it was found that the pills left the stomach according to their size. In mild cases of spasm papaverin was found to be effective in definitely shortening the time of exit of the pills; in severe cases it lessened vomiting but did not facilitate the passage from the stomach.

16 West Eighty-Sixth Street.

THE FREQUENCY OF INFECTION WITH THE TUBERCLE BACILLUS IN CHILDHOOD *

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A statement in one form or another that 90 per cent. or more of children are infected with the tubercle bacillus by their fourteenth year has frequently appeared in both the medical literature and the lay press of the last few years. This is one of the factors which has been urged in support of the theory that the pulmonary tuberculosis of early adult life is a lighting up of an old latent infection acquired during childhood—a possible but as yet unproved hypothesis. In tracing back the authority for this statement we find that it is almost entirely based on the figures of Hamburger and Monti,¹ who made tuberculin tests on 532 children convalescing from diphtheria and scarlet fever in the wards of a public hospital in Vienna. These children were first tested by the cutaneous method, and if the reaction was negative, 1-100 milligram, or more, of tuberculin was injected and the subcutaneous local (*Stich*) reaction recorded. Positive tuberculin tests are regarded as evidence of infection with the tubercle bacillus, whether the tuberculosis be active, latent or healed. The detailed results of their tests are shown in Table 1.

TABLE 1.—CHILDREN SUBMITTED TO TUBERCULIN TEST (HAMBURGER AND MONTI)

| Age (Years) | No. Children | Positive Reactions | Per Cent. Positive |
|---------------|--------------|--------------------|--------------------|
| Under 1 | 23 | 0 | 0 |
| 1-2 | 46 | 4 | 9 |
| 2-3 | 56 | 11 | 20 |
| 3-4 | 75 | 24 | 32 |
| 4-5 | 50 | 26 | 52 |
| 5-6 | 63 | 32 | 51 |
| 6-7 | 46 | 28 | 61 |
| 7-8 | 30 | 22 | 73 |
| 8-9 | 35 | 25 | 71 |
| 9-10 | 26 | 22 | 85 |
| 10-11 | 29 | 27 | 93 |
| 11-12 | 19 | 18 | 95 |
| 12-13 | 17 | 16 | 94 |
| 13-14 | 17 | 16 | 94 |

* From the Department of Pediatrics, Washington University Medical School, and the St. Louis Children's Hospital.

¹ Submitted for publication, April 5, 1915.

1 Hamburger and Monti: München med. Wchenschr., 1909, lvi, 449.

No one else has reported such a high incidence of infection among children free from clinical tuberculosis. In fact, von Pirquet,² to whom credit must be given for first showing the frequency of infection with the tubercle bacillus in childhood, obtained lower figures among the same class of children in Vienna even when cases of clinical tuberculosis were included in his statistics. Von Pirquet used only the cutaneous test in determining the presence of an infection. In Table 2 his figures are given in a condensed form for various age periods. In the second part of the table the figures give the percentage of positive reactions in children free from clinical manifestations of tuberculosis.

TABLE 2.—RESULTS OF CUTANEOUS TESTS (VON PIRQUET)

| Age (Years) | Including Cases of Tuberculosis | | | Excluding Cases of Tuberculosis | | |
|-------------|---------------------------------|--------------------|-----------|---------------------------------|--------------------|-----------|
| | Total No. | Positive Reactions | Per Cent. | Total No. | Positive Reactions | Per Cent. |
| Under 1 | 410 | 21 | 5. | 388 | 0 | 0. |
| 1-2 | 116 | 24 | 20. | 89 | 0 | 0. |
| 2-4 | 208 | 74 | 35. | 162 | 22 | 13. |
| 4-7 | 264 | 127 | 48. | 189 | 53 | 30. |
| 7-10 | 216 | 138 | 64. | 154 | 74 | 48. |
| 10-14 | 193 | 155 | 80. | 147 | 105 | 70. |

The figures of both Hamburger and von Pirquet were obtained from tests made on children of the poorer classes of society in Vienna—a city where tuberculosis is notoriously frequent—and who were living in an environment which is only found in the slums of the older continental cities. As von Pirquet said, "In other cities it (the percentage) will hardly be as high . . ."³

In the course of our work at the St. Louis Children's Hospital we gained the impression that positive tuberculin reactions were much less frequent than might be expected from the general idea which prevails, although we were dealing with children of relatively the same class as Hamburger, as our patients are all from the poorer and more congested districts of St. Louis. In order to see whether this was an impression or a fact, the clinical records of the past three years were carefully gone over and the results of the tuberculin tests tabulated. As our results gave figures so different from the general impression of the frequency of infection, and as we have been unable to find any reports of large series of tests on children in American cities, it has seemed of sufficient interest to place our statistics on record. Our figures do not represent a special study of the frequency of tuberculin reactions in childhood, but the results of tests made for diagnostic purposes on hospital patients regardless of the cause for their admission. Tuberculin tests are made on all infants under two

2. Von Pirquet: Jour. Am. Med. Assn., 1909, lii, 675.

3. Von Pirquet: Trans. VI Internat. Cong. Tuberc., 1908, ii, 559.

years admitted to the hospital as a part of the routine examination, but the tests in older children do not represent consecutive admissions. As a rule tests are only made in children over two years when there is some indication. In Table 3 the figures include all cases, and in Table 4 the cases with *clinical manifestations of tuberculosis have been deducted*. As all of these children were admitted to the hospital for some pathologic condition, it is very probable that the figures in Table 4 are higher than would be obtained if an examination of "normal school children" of the same social conditions were made. The cutaneous test of von Pirquet was used in all cases. Full strength "old tuberculin" was used and the scarification made through drops by means of a von Pirquet scarifier. Whenever a reaction was questionable a second test was made. The activity of the tuberculin was frequently checked by tests on known cases of tuberculosis which had previously given positive reactions. As the children were in the hospital no difficulty was experienced in observing and recording the reaction at various intervals after the test was applied. For the last six months we have followed negative cutaneous reactions with intradermic injections of 1/100 and 1/10 mg. of tuberculin, as the cutaneous test is regarded by Hamburger as only being positive when the individual has a degree of sensitiveness which reacts to 1/1,000 of a mg., or less, injected intradermally.⁴ Hamburger contends that the subcutaneous local and the intradermal reactions are from 25 to 30 per cent. more delicate than the cutaneous test of von Pirquet, but in 263 cases tested in this way the increased percentage of positive reactions was only 10 per cent. and not 25 to 30 as Hamburger found. We may therefore regard these children in our series tested by the cutaneous method alone as giving a very fair estimate of the extent of infection with the tubercle bacillus among the children of the lowest strata of society in St. Louis. The fact that the children in our series were hospital patients accounts for the large amount of clinical tuberculosis. This is especially the case for the figures for the first year of life.

TABLE 3.—TOTAL REACTIONS INCLUDING CASES OF CLINICAL TUBERCULOSIS

| Age (Years) | No. Children Tested | Positive Reactions | Per Cent. Positive |
|---------------|------------------------|-----------------------|-----------------------|
| Under 1 | 224 | 25 | 11 |
| 1-2 | 137 | 34 | 24 |
| 2-4 | 188 | 57 | 30 |
| 4-6 | 206 | 68 | 33 |
| 6-8 | 182 | 74 | 40 |
| 8-10 | 157 | 69 | 44 |
| 10-12 | 115 | 45 | 40 |
| 12-14 | 112 | 54 | 48 |
| | 1321 | 426 | |

4. Hamburger: Die Tuberkulose des Kindesalters, 1912, p. 62.

TABLE 4.—REACTIONS IN CHILDREN WITHOUT CLINICAL MANIFESTATIONS OF TUBERCULOSIS

| Age (Years) | No. Children Tested | Positive Reactions | Per Cent. Positive |
|-------------|---------------------|--------------------|--------------------|
| Under 1 | 202 | 3 | 1.5 |
| 1-2 | 109 | 6 | 5.5 |
| 2-4 | 163 | 32 | 19 |
| 4-6 | 172 | 40 | 23 |
| 6-8 | 152 | 44 | 29 |
| 8-10 | 126 | 38 | 30 |
| 10-12 | 107 | 37 | 34 |
| 12-14 | 94 | 36 | 38 |
| | 1125 | | |

From these tables it will be seen that the percentage of positive tuberculin reactions among children of relatively the same social conditions was much lower in St. Louis than in Vienna. For purposes of comparison we have grouped the percentages of positive reactions into age periods in Table 5. These figures are for children without clinical tuberculosis.

TABLE 5.—PERCENTAGE OF POSITIVE REACTIONS GROUPED BY AGE PERIODS

| Age (Years) | St. Louis | Vienna | |
|-------------|-----------|-------------|-----------|
| | | von Pirquet | Hamburger |
| Under 1 | 1.5 | 0 | 0 |
| 1-2 | 5.5 | 0 | 9 |
| 2-4 | 19 | 13 | 26 |
| 4-7 | 25 | 30 | 54 |
| 7-10 | 30 | 48 | 75 |
| 10-14 | 36 | 70 | 94 |

In St. Louis the increase after the 2 to 4 year age period is relatively slow, while in Vienna this corresponds to the period of most rapid increase.

In a cursory search of the literature we were surprised to find the few series of cases reported in view of the importance and publicity that has been given to the figures of Hamburger. In America Shaw and Laird⁵ tested 330 institutional children and found a maximum of 45 per cent. giving positive reactions between the ages of 6 and 14. Wachenheim⁶ obtained but 5 positive reactions among 80 non-tuberculous children from the congested districts of New York. Several larger series of tests among infants and young children have been reported. We have found a number of reports from European cities and it is noticeable that among these Hamburger's figures give the highest percentage of positive reactions. Overland⁷ tested 843 school children in Bergen and found the positive reactions reached a maximum of 50 per cent. at the 12 to 14 year age period. In nearly rural

5. Shaw and Laird: *Trans. Nat. Soc. Study and Prev. Tuberc.*, 1909, v, 350.

6. Wachenheim: *Am. Jour. Dis. Child.*, 1913, v, 466.

7. Overland: *Abstr. in Internat. Centralb. f. Tuberk.*, 1914, viii, 818.

districts the incidence of infection was considerably less. Stawsky⁸ found the infections reached about 60 per cent. between the ages of 12 and 16 years in Odessa. Amenta⁹ in Palermo tested 800 children under 12 years by the cutaneous method and found a rather higher incidence: 0-6 months 17.5 per cent.; 6-12 months 30 per cent.; 1-2 years 28 per cent.; 2-4 years 47.5 per cent.; 4-6 years 72 per cent.; 6-8 years 75 per cent.; 8-12 years 83 per cent. Calmette, Grysez and Letulle¹⁰ reported tests on 1,226 children in Lille and found positive reactions in 81 per cent. between the ages of 5 and 15.

It is thus seen that there is no uniformity in the figures obtained in different countries and cities, a condition which can hardly be attributed to faulty or differences in technic with such a simple procedure as the cutaneous tuberculin test. As a matter of fact, one would hardly expect to obtain uniform figures, as the incidence of tuberculosis is such an accurate index of social and living conditions, and these factors differ so widely in different communities. For example, the death rate for all forms of tuberculosis per 100,000 of population in St. Louis in 1910 was 184, while in Vienna the death rate for pulmonary tuberculosis alone was 249 per 100,000. That the extent of infection in childhood bears a relationship to the degree of exposure to clinical tuberculosis has been shown by Sachs and others, and more recently by Lamson. Lamson¹¹ found that 67 per cent. of individuals in families in which there was an open case of tuberculosis showed evidences of infection with the tubercle bacillus. In families in which there was "latent" tuberculosis, 22 per cent. showed evidences of infection, and in families in which there was no tuberculosis, only 2½ per cent. We have been unable to find a report of a series of tuberculin tests on children of families living in the better residential districts of our large cities, but there is every reason to believe that the extent of the infection is much less than is found in the congested districts. The extent of the infection with the tubercle bacillus in childhood is in all probability directly proportionate to the amount of tuberculosis in a given community, and to the degree of intelligence to which people are educated regarding the dangers of, and the method of preventing, the spread of tuberculosis.

It is quite possible that the extent of infection among certain classes may reach 90 per cent. by the fourteenth year, but this is extreme, and most statistics give much lower figures. It must be kept in mind that all of the figures which have so far been published are from hospital or dispensary children. It would be well worth while if some one

8. Stawsky: Abstr. in *Internat. Centralb. f. Tuberk.*, 1914, viii, 821.

9. Amenta: Abstr. in *Internat. Centralb. f. Tuberk.*, 1914, viii, 632.

10. Calmette, Grysez and Letulle: *Presse méd.* 1911, xix, 651.

11. Lamson: *Studies in Public Health*, Univ. of Minnesota, 1913.

with an extensive private practice among the better classes of society would publish the results of a large series of tests. It would seem, however, that although infection with the tubercle bacillus is widespread, the usual statements as to the extent of the infection as a whole are gross exaggerations.

Although not strictly germane to the subject of this report, it may not be amiss to express the opinion we have formed in the course of our work in regard to the value of the tuberculin test as a diagnostic measure in childhood. Positive reactions in early childhood and infancy are generally regarded as of value. With this we concur. The statement is then usually made that the tests are of little or no value in older childhood (from 3 to 7 years on, according to various observers) as the latent infections are so numerous by this time. From our figures it will be seen that latent infections are not so common in St. Louis as has been inferred from the statistics from other cities. As far as negative reactions in clinical cases of tuberculosis are concerned, we have met with but six cases of tuberculin insensitiveness. Five of these were in children with high temperatures, tested shortly before death occurred, and the sixth was a case of old, long-standing abdominal tuberculosis in which a mesenteric gland removed at operation showed tubercles on histologic examination. In this connection it is interesting to note that several cases of "hip joint" disease on the orthopedic service of Dr. Allison, which were at first regarded as tuberculous, but which gave repeated negative tuberculin tests, subsequently proved to be cases of osteochondritis juvenilis (Perthes disease). Even if latent infections are frequent enough to lessen the diagnostic value of positive tuberculin reactions, they have not infrequently given support to the data obtained on physical examination in the diagnosis of a tuberculous process. Furthermore, we are of the opinion that sufficient emphasis has not been placed on *negative* tuberculin tests in older childhood, particularly in children with pulmonary lesions. The clinical similarity between pulmonary tuberculosis and chronic influenzal and pneumococcic processes in older children is very marked, and in the diagnosis of these conditions we have found negative tuberculin reactions of great aid.

SUMMARY

A study of tuberculin tests in 1,321 hospital children in St. Louis shows that the percentage of positive reactions reaches a maximum of 44 per cent. at the age period of 10 to 14 years, including cases with clinical tuberculosis. If children with clinical tuberculosis are excluded the percentage giving positive reactions at the 10 to 14 age period is only 36. These figures are much lower than the usual "90 per cent."

figure for the incidence of infection with the tubercle bacillus in children by their fourteenth year, which has gained such widespread publicity and which is based on the figures of Hamburger for Vienna.

The extent of infection among children varies in different cities and countries and is dependent on such factors as living and social conditions, the amount of tuberculosis in the community, the exposure of the child to open tuberculosis, and in all probability varies among different classes of society in the same community. No conclusions as to the extent of infection with the tubercle bacillus can be drawn from the statistics of any one city or class, and the statement that "90 per cent. or more" of individuals are infected by puberty is an extreme exaggeration of the actual conditions which exist.

The intradermic tuberculin test has given but a slight increase in the percentage of positive reactions over the percentage of positive cutaneous reactions. We have found that positive tuberculin reactions are of much service in the diagnosis of tuberculosis in infancy and early childhood, and that both positive and negative reactions in conjunction with the physical signs and symptoms have been of diagnostic value in individual cases among older children, although as a whole they do not indicate whether the infection is active or latent.

A CASE OF BILATERAL GLIOMA OF THE RETINA *

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The facts concerning the origin, course and prognosis of the non-pigmented cancer of the retina occurring in children are well known. Wintersteiner's classical monograph, in which he describes 467 cases, has been referred to as a basis of their remarks by authors who have published accounts of individual cases. Wehrli¹ believes that retinal hemorrhages are the prime etiologic factor, because he has found rosettes, the centers of which were formed by the smallest vessels. These vessels were fully developed and for the most part degenerated, while their lumen contained remnants of red blood corpuscles surrounded by epithelial-like tumor cells.² Lindenfeld³ in the study of the normal eyes of the fetus speaks of "granular rosette folds and folds of undifferentiated cells. From the cells may be derived the similarly arranged cells of retinal glioma." Fuchs⁴ description of the pathology and changes voices the generally accepted opinion:

It develops ordinarily from two granular layers of the retina. The tumor is composed of small, cylindrical, epithelial cells and a soft basement substance. In many cases the cells are arranged about an open space, like the cross section of a gland tubule. The multiplication of the tumor cells takes place mainly in the immediate vicinity of the numerous wide blood vessels. Here are the youngest cells which displace the older cells, the latter undergoing necrosis. Neoplasm germs pass from the degenerated retina into the choroid and vitreous, where they subsequently develop into small independent nodules.

In considering the etiology, heredity should be given an important place. Many are the instances recorded in which the disease has manifested itself in the parents and children, or in several children of the same parents. Fuchs⁴ says, "A congenital morbid disposition very often lies at the bottom of glioma" and illustrates his statement by the following history: a 4 year old boy with advanced and perforating glioma of the right eye; a 2 year old brother with glioma of the right eye; finally a child of the same parents a few months old, with typical congenital coloboma of the iris and choroid. De Gouva⁵

* Read before the Section on Ophthalmology, College of Physicians, Philadelphia, March 18, 1915.

1. Wehrli: *Græfe's Arch. f. Ophthal.*, 1909, p. 504.

2. *Ophth. Year Book*, 1910.

3. Lindenfeld: *Klin. Monatsb. f. Augenh.*, April, 1913.

4. Fuchs: *Text Book*, edited by Duane.

5. De Gouva: On the Heredity of Glioma of the Retina, *Ann. d. Oculist*, January, 1910, cxliii.

removed the right eye of a 2 year old boy for glioma in 1872. There was no recurrence, and on growing up he married a woman in whose family there was no tendency to the formation of neoplasm. They had seven children, the second and third of whom, both girls, died of double retinal glioma. Von Hoffman, Jr.,⁶ and Owens⁷ recorded other instances.

The list of affections which may be confounded with glioma and, which are usually classified under the unexpressive and negative term of "pseudoglioma," is appallingly large, and the diagnostician who endeavors to be accurate and specific cannot be satisfied with the two classes of glioma and pseudoglioma. Curtil⁸ enumerates the affections to be differentiated: metastatic ophthalmia, especially in the form of exudative choroiditis; metastatic or traumatic exudative or suppurative lesions of the vitreous; choroidal tuberculosis; simple detachment of the retina; certain congenital anomalies; cysticercus of the deep membranes of the eye.

It is not enough to say prior to dismissing the subject of differentiation that the history and clinical symptoms of true glioma would indicate the diagnosis. While this may be true in some of the diseases mentioned, it is not true for all. Simple retinal detachment, for example, rarely occurs spontaneously. Malignant myopia, traumatism or constitutional affections, usually point to the etiology. Moreover, the separated retina is wavy, its arteries and veins of the same dark color and readily seen, and when transillumination may be employed, throws no dark shadow. Metastatic choroiditis has a distinct history, occurs at any age, is rapidly progressive, and has a dark yellow or reddish color and not the almost pink white of glioma. Advanced choroidal tuberculosis is almost never found in very young children and may be regarded as a local sign of general tuberculosis.

Congenital anomalies remain unchanged in their appearance for many years. Cysticercus may be diagnosed in most instances with the ophthalmoscope. Friedenwald⁹ and de Schweinitz¹⁰ cite cases of "retinitis with massive exudation" that resemble glioma in their ophthalmoscopic appearance. They are essentially different in their etiology, history and course and will not be confused by the thoughtful observer. In a case recorded by Krauss¹¹ and in others to which he refers in his paper, the diagnosis is more difficult. A boy of 8 received an injury to the eye at birth. Seven months before examination, and

6. Von Hoffman, Jr.: Heidelberg Congress, 1908.

7. Owens: Royal London Ophth. Hosp. Rep., 1905.

8. Curtil: Rev. gén. d'ophtal., Dec. 31, 1910.

9. Friedenwald: Trans. Am. Ophth. Soc., 1914, xii, Part iii.

10. de Schweinitz: Trans. Am. Ophth. Soc., 1914, xii, Part i.

11. Krauss: Ophthalmology, April, 1913.

several times since, there had been signs of moderate inflammation. The pupil was dilated and fixed, anterior chamber shallow and a few posterior synechiae were present. A greenish-yellow reflex shone from behind the lens on the temporal side, and later, all around the pupil. The eye was enucleated. There was total retinal detachment, subretinal hemorrhages and a mass of partly organized inflammatory exudate between the retina and the lens. The blood vessels of the retina were degenerated but the iris, choroid and sclera were practically normal. I believe his case belongs to a special group properly called "pseudoglioma" which originates primarily in the retina. I agree with those who hold that there is a distinct disease of the retina occurring in children which produces clinical symptoms closely simulating glioma and is of retinal and not choroidal origin. Even in Krauss' case real glioma might be excluded before enucleation on account of the age of the patient, the recurring attacks of inflammation and the absence of the signs of secondary glaucoma.

Devereux Marshall states that the statistics of the Moorfields Hospital show that about 60 per cent. of the cases of glioma occur in the first two years of life and that about 80 per cent. occur during the first three years. He studied thirty-two cases; of these there were fifteen which had exceeded the three year limit, the time running from three years and four months to six years and nine months. Wintersteiner found 75 per cent. within the first three years. Curt Adam¹² studied the records of forty-seven cases. All the patients were less than 12 years old, 94 per cent. being under 4 years. The attacks of inflammation, the posterior synechiae and the yellowish-green foreign material in the posterior chamber, and the absence of secondary glaucoma, point to retinal or choroidal inflammation rather than a glioma.

CASE REPORT

History.—Boy 2 years old. Parents healthy. No family history of cancer or other forms of tumor or of congenital affections of the eyes. The patient has a sister two years older than himself who is apparently well and strong. One year ago a "shine" was noticed in the pupil of the left eye. At present the eyeball is larger than its fellow, the pupil dilated and immobile, anterior chamber shallow, lens clear and the entire vitreous occupied by a shining, white, irregular mass, traversed by a few blood vessels. Tension +1. No perception of light. Under chloroform anesthesia, and through the pupil dilated with homatropin, a small, round, white mass projecting several diopters into the vitreous and situated close to the nerve head on its temporal side was seen in the *right* eye. An object held in the center of the field of fixation was not seen by the child, but even small objects were readily perceived in the periphery. The left eye was enucleated. The pathologist's report is as follows:

Pathologist's Report.—The specimen is that of an eyeball with attached portion of optic nerve. It measures 2.8 by 2.1 cm. and weighs 3.8 gm. The eyeball is soft and the anterior chamber is partly collapsed. There is no apparent

12. Adam, Curt: *Ztschr. f. Augenh.*, 1911, xxv, 330.

external evidence of disease, except for a marked grayish opacity of the lens. On section, after hardening the eyeball, an irregularly outlined, grayish, soft tumor mass occupies the vitreous, apparently arising near the entrance of the optic nerve and extending into the vitreous to within a few millimeters of the lens. This mass measures 1.4 by 0.9 cm. in its greatest diameters. The retina everywhere appears to be intact.

Histology: The sections show the tumor mass apparently arising from the granular layers of the retina, and made up of numerous small round cells with deeply staining nuclei lying amongst a fairly abundant network of neuroglia fibers. The blood vessels, with well formed walls and filled with red cells, appear directly amongst the cellular elements. The tumor growth has not involved the optic nerve.

Diagnosis: Glioma of retina.

Subsequent Course.—Three weeks later the left orbit was fitted with an artificial eye. The tumor in the right eye had increased in size and vision was measurably reduced. It was my distasteful duty to inform the parents that enucleation of the right eye must be performed as soon as vision should be lost, because by this means only was there a chance of saving the child's life.

My situation was exactly that described by Jacqueau¹³ and doubtless experienced by all who have had cases of bilateral glioma to deal with. He emphasized the tragic dilemma of the surgeon who is called on to render a decision in such cases. Van Duyse¹⁴ in discussing Gallemaert's case of double glioma says that even in such instances the patient may survive if enucleation has not been delayed too long. He referred to a case of his own in which fourteen months had elapsed without recurrence since enucleation of the second eye, which had been removed two years after the first.

Postponement of enucleation is fatal. Once the diagnosis is established, sentimental objection by parents, and alas! sometimes by the family physician, should be given no serious consideration. The disease will surely spread, either by rupture of the sclera and extension to the orbital contents, or posteriorly along the nerve, and then enucleation or even evisceration would be useless. Spontaneous cure cannot be expected, notwithstanding Lindenfeld's¹⁵ experience, who reports a case of spontaneous cure, the third of its kind to be supported by pathologic findings. He saw a 4 year old child with fungoid glioma of the right eye and a shrunken left globe. Both eyes were enucleated. The clinical diagnosis of bilateral glioma was confirmed histologically only as regards one eye, since no trace of glioma could be demonstrated in the shrunken eye. But the belief that this eye had previously suffered from the same condition was established by the entire clinical history and course of the disease. The "spontaneous cure" was due to complete necrosis of the tumor. This "pathologic cure" is to my mind even worse than enucleation.

13. Jacqueau: Clin. Ophth., 1912, xix, 733.

14. Van Duyse: Soc. Belge d'ophth., 1911, xxv, 19.

15. Lindenfeld: Graefe's Arch. i. Ophthal., 1912, lxxxvi, 141.

In the bilateral cases, which constitute about 25 per cent. of the total number, the disease begins in one eye and the second eye is involved some months later. The question arises whether prompt enucleation would save the second eye. In other words, could the second eye become involved by sympathy?

In this connection the four cases reported by Ayers¹⁶ are of interest: 1. Enucleation was performed when the tumor had advanced to the cornea and quite filled the globe. The patient is now 14 years of age and in good health. 2. The eye was enucleated after blindness of several months. "This child is now 8 years old and in excellent health." 3. The tumor was almost in contact with the lens, the pupil dilated, and T+1. The child died two weeks after enucleation from extension of the growth into the brain. 4. Enucleation. "The child is now 2½ years old and bids fair to pass the three years' limit of immunity."

These histories emphatically negative the supposition that the sound eye is involved sympathetically.

Glioma may be briefly described as a malignant tumor arising from the granular layers of the retina, almost pure white, traversed by a few blood vessels, steadily advancing, without pain or symptom of constitutional irritation, until it has reached its second or glaucomatous stage. Unless the eyeball is enucleated, the tumor will perforate the coats of the eye and invade the orbit, or it will travel backward in the optic nerve and invade the brain. The only conservative treatment is the enucleation of the eye at the earliest moment. By this means the second eye may not be involved and the life saved. De Kleijn¹⁷ states concerning four cases in which the optic nerve was microscopically free from disease at the time of operation, that the subsequent records show no fatalities. When the optic nerve was affected but not up to the point of division, two patients had been well for eight and seven years, respectively, and four had died. Of five cases in which the optic nerve was affected at the point of section, only one patient had lived, the interval since operation being four years. The three-year limit is generally accepted. Statistics show that fatalities occur as a rule within the first year, and should the patient survive without recurrence until the termination of the third year, the prognosis is favorable.

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16. Ayers: *Arch. Ophthalm.*, July, 1906.

17. De Kleijn: *Arch. f. Ophthalm.* (Graefe's), 1911, lxxx, 371.

CLOTHING AS A FACTOR IN THE PRODUCTION OF HEAT STASIS *

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The studies of the relation of heat to the high infant mortality of summer have not yielded uniform results. A more careful review of the procedures which have been employed in these studies readily explains these contradictory conclusions. The external factors, such as food, high outdoor and indoor temperatures, circulation of air, etc., have received most of the attention; while the most important internal factor, i. e., the heat regulatory power of the infant, has been neglected by most authors. The question, then, which confronts us is: the reaction of the infant to the changes in its environment, with special reference to its heat regulation.

Heat equilibrium of the organism depends on the proper balance between:

I. Heat production,

II. Heat elimination.

I. Heat production is influenced chiefly by:

1. Food,

2. Work.

1. That food can influence heat production is shown by Rubner,¹ who was able to increase the heat production of a dog 44 per cent. by excessive feeding. A food, the caloric value of which meets the requirements of the organism at a moderate temperature, may become excessive in summer if the heat loss is interfered with. This may be further emphasized by the composition of the food.

2. That muscular activity increases heat production has been very well known, for instance, by Howland's² calorimetric observations on infants. He has shown that the heat production of infants, crying or making active movements, is considerably greater than that of those asleep.

II. Heat Elimination. Heat loss is dependent almost entirely on:

1. Radiation.

2. Conduction.

3. Evaporation.

* Submitted for publication March 25, 1915.

From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital.

1. Rubner: *Lehrbuch der Hygiene*, 1907. Ed. 8.

2. Howland: *The Scientific Basis for the Artificial Feeding of Infants*, *AM. JOUR. DIS. CHILD.*, 1913, v, 390.

1 and 2. Loss by radiation and conduction is proportional to the difference between the surface temperature of the body and that of the surrounding air. As the temperature of the air approaches that of the body surface, the loss due to these two factors becomes less. It is zero at temperatures equal to or above that of the body surface.

Good circulation of air aids heat loss by conduction and radiation, by a more frequent exchange of air strata about the individual. The surface temperature of the clothing is less than that of the uncovered body and, therefore, approaches more nearly that of the external air. This fact accounts for the less rapid loss of heat through radiation and conduction in clothed individuals.

3. Evaporation gains in importance as a means of heat loss at high temperatures, coincident with the appearance of visible perspiration, and becomes the principal means of heat loss when the temperature of the surrounding air is higher than that of the body. Evaporation is increased by good circulation of the air and inhibited by high humidity. One must not lose sight of the fact, however, that water is constantly lost through the skin independently of the action or presence of sweat glands. This has been clearly shown by Loewy³ in a recent publication, in which he reports observations on the loss of water from the skin in three individuals who had a peculiar ectodermal anomaly, in that the sweat glands, and to some extent the sebaceous glands, were absent. At moderate temperatures, with the body at rest, the loss of water from the skin of these individuals was as great as that from the surface of normal individuals. From this he considers the so-called insensible perspiration a physical, not a physiologic phenomenon. The work of Galeoti and Macri,⁴ although their method is not free from objection, seems to add some support to this view. They found that the loss of water by insensible perspiration on the different portions of the skin of the same normal individual is not proportional to the number of sweat glands present there.

Mendelssohn⁵ studied heat regulation of the infant and found this mechanism to be more efficient at high than at low surrounding temperatures. He also emphasizes the importance of heat loss by evaporation from the skin and lungs at high temperatures (e. g. 40 C.). He calls attention to the increased respiratory rate at these temperatures and states that at such temperatures heat loss by radiation and con-

3. Loewy: Untersuchungen über die physikalische Hautwasserabgabe, *Biochem. Ztschr.*, 1914, lxxvii, 4, 5, p. 243.

4. Galeoti and Macri: Ueber die Perspiratio Insensibilis unter normalen und pathologischen Bedingungen, *Biochem. Ztschr.*, 1914, lxxvii, 6, p. 472.

5. Mendelssohn: Ueber das Wärmeregulationsvermögen des Säuglings, *Ztschr. f. Kinderh.*, 1913, v, 269; Beobachtungen über Hauttemperaturen der Säuglinge, *Ztschr. f. Kinderh.*, 1912, iii, 292.

duction is relatively unimportant. He states, however, that in the majority of infants no sensible perspiration was noted. He mentions the prophylactic value of cool surroundings and scant clothing during hot weather. Rubner had previously shown the importance of heat loss by evaporation from the skin and lungs at high temperatures.

Rietschel,⁶ Kleinschmidt,⁷ Liefmann and Lindemann⁸ and others, and more recently Helmholz,⁹ have studied the relation of high indoor and outdoor temperatures to infant mortality. Helmholz made careful observations on forty-six infants, extending over a period of eight summer weeks. These infants attended infant welfare stations in Chicago, and were considered fairly normal tenement babies. Their feedings were supervised by the infant welfare physicians, who also gave advice concerning hygiene. A nurse visited the homes each day. Rectal temperatures and maximal and minimal room temperatures were recorded daily. Notes were also made on the stools and general condition of the infants. Helmholz's observations show no definite relationship between individual high room temperature readings and individual cases of hyperthermia and gastro-intestinal disturbance. He says: "The direct effect of heat alone must be considered of relatively little importance. Infants can tolerate temperatures decidedly above those usually supposed to be harmful, without any bad effects; in fact, can gain in weight during such time." He points out that in his cases heat, humidity and diet were quite uniform and that certain infants showed ill effects even at relatively low temperatures, a fact which requires the investigation of other factors allowing greater individual variability. "Such a factor we have in clothing."

This work of Helmholz and the fact that food, temperature, humidity and ventilation have been investigated to a considerable extent, has led us to undertake an experimental study of the effect of clothing—a factor which has received relatively little attention, and which can, in various ways, influence heat loss.

EXPERIMENTAL PROCEDURE

In each of eight experiments two puppies of the same litter, ranging in age from 4 to 6 weeks, were put into an incubator in which was maintained a temperature simulating that of a hot summer. A jacket was placed on one of the puppies in the incubator; the other remained uncovered. In six of the experiments an additional control puppy wearing a jacket was kept at room temper-

6. Rietschel: Sommerhitze, Wohnungstemperatur und Säuglingssterblichkeit, *Zschr. f. Kinderh.*, 1911, i, 546.

7. Kleinschmidt: Der Einfluss der Hitze auf den Säuglingsorganismus, *Monatschr. f. Kinderh.*, 1910-11, ix, 455.

8. Liefmann and Lindemann: Der Einfluss der Hitze und die Sterblichkeit der Säuglinge in Berlin, etc., *Vierteljahrh. f. öff. Gesundheitspflg.*, 1911, xviii, 333.

9. Helmholz: The Relation of Heat to the Morbidity and Mortality of Infants from Gastro-Intestinal Diseases, *Jour. Am. Med. Assn.*, 1914, lxiii, 1511.

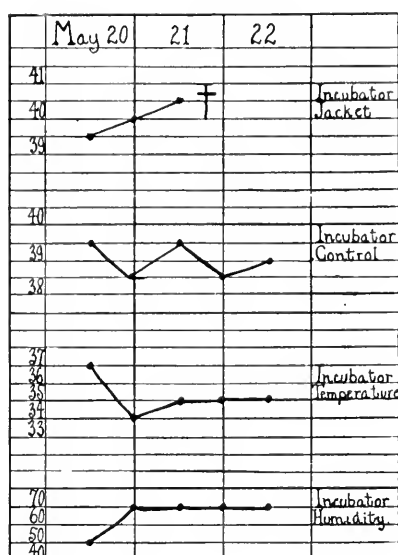


Fig. 1.—(Experiment 1.) Rectal temperatures of incubator puppies (jacketed and control), the incubator temperature and humidity, etc. The plus sign indicates the death of the animal. This explanation applies to all of the following charts.

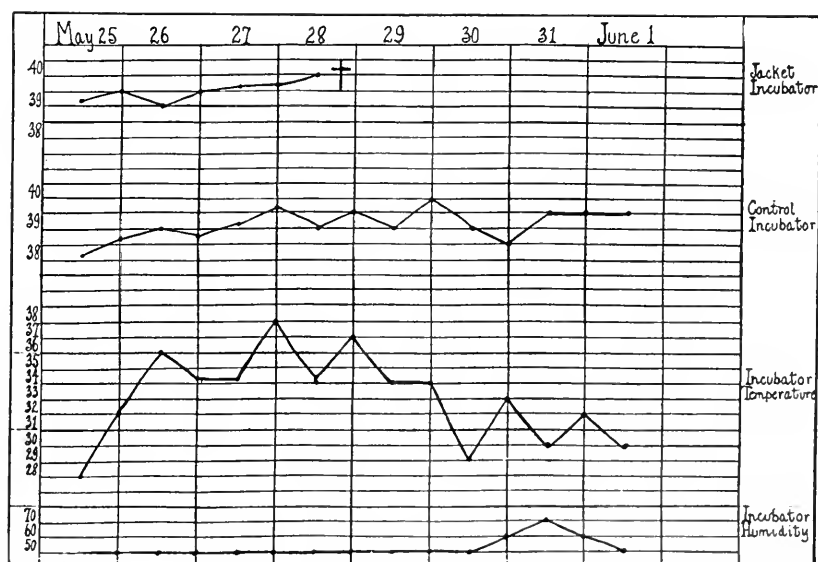


Fig. 2.—Experiment 2.

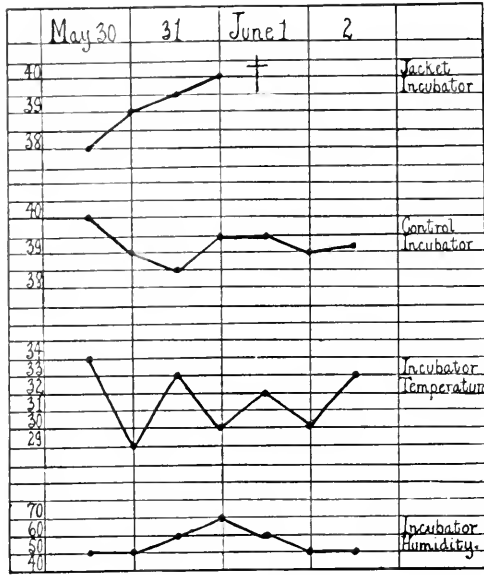


Fig. 3.—Experiment 3.

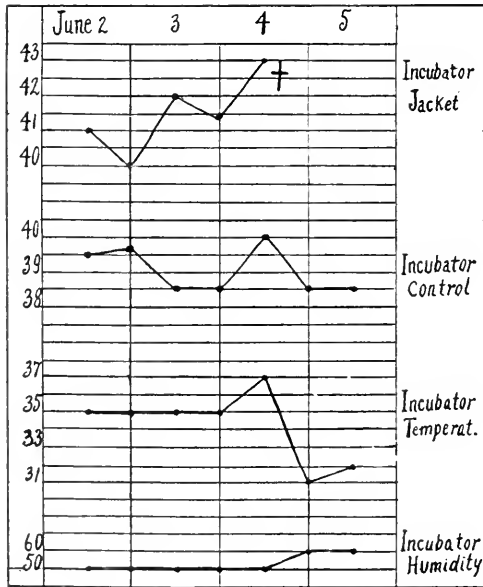


Fig. 4.—Experiment 4.

ature. In a seventh experiment, one without a jacket served as an outside control. Observations were made on the incubator temperature and humidity, and also on the puppies' rectal temperatures. The stools and the general condition of the puppies were also noted. The animals in each experiment received equal amounts of milk as the only food. They were usually fed from the bottle, having been weaned shortly before the experiment began. Water was given freely.

Jackets.—The jacket (except in Experiments 1 and 2, see protocols) was made of two layers of Canton flannel, sewed about the trunk, shoulders and hips of the puppy. The head, upper part of the neck, legs and tail were uncovered. A single layer of adhesive plaster was placed over the flannel to make it fit more snugly. The jackets allowed freedom of movement and respiration.

Incubator.—The incubator was one that had been previously used for premature infants. The temperature in this incubator is maintained by a hot water pan, heated from without by means of a gas burner. The automatic temperature control was not especially accurate. In addition, it was necessary to open the door at periods for feeding, temperature taking and cleaning. No special measures were taken to regulate the humidity nor to insure ideal ventilation. The latter depends on an air inlet of 7 cm. diameter at the bottom of the incubator, and an outlet flue of the same diameter at the top of the chamber.

The accompanying charts show the rectal temperatures of the incubator puppies (jacketed and control), the incubator temperature and humidity; + indicates the death of the animal.

Reference to the charts shows that in each one of the eight experiments the jacketed animal died, hyperthermia being noted in each instance. In Experiments 1, 2, 3, 4, 7 and 8, the jacketed animal died within eighty-four hours. It is seen also that the rectal temperature of the incubator jacketed puppy was usually higher than that of the incubator control animal. In Experiment 5 and Experiment 6 the jacketed animals seemed considerably more resistant, the puppy in Experiment 5 living ten days, during which time two control animals died. In Experiment 6 the animal lived nine days, in which period one control puppy succumbed. In Experiment 5 the first control puppy was unusually fat, the second showed ill effects almost immediately after being put into the incubator and died within twenty-four hours. The first control animal in Experiment 6 showed blood in the stools a few hours before death and at post mortem an intussusception was found about 5 cm. long in the ascending colon. The visceral peritoneum was not adherent but the mucosa was found somewhat necrotic. A dark red area was found about 5 cm. further along in the intestine. It will be seen that the last rectal temperatures before death in the control dogs of Experiment 5 were relatively low compared with those of the other fatal cases.

The control puppies with jackets at room temperature seemed normal. The room temperature was usually about 9° C. lower than that of the incubator. The rectal temperature of these outside control animals was usually about 0.8° C. lower than that of the incubator control animals, and 1.4° C. lower than that of the incubator jacketed puppies.

Stools.—No striking differences were noted in the condition of the stools of the various animals. The stools of the incubator animals were somewhat more frequent and looser than those of the outside control puppies.

Post-Mortem Findings.—Post mortems were made on all puppies which died. (Eight jacketed incubator puppies; three control incubator puppies.)

The principal macroscopic findings were as shown in Table 1.

TABLE 1.—MACROSCOPIC FINDINGS POST MORTEM

| Organ | Jacket Incubator Puppies Cases | Control Incubator Puppies Cases |
|---|--------------------------------------|---------------------------------------|
| Brain— | | |
| Hyperemia of the meninges..... | 7 | 2 |
| Hyperemia of the cortex..... | 7 | 2 |
| Skull not opened..... | 1 | 1 |
| Thymus— | | |
| Petechial hemorrhages just beneath the surface | 6 | 3 |
| Lungs— | | |
| Hyperemia | 6 | 3 |
| Spleen— | | |
| Soft, deep purple | 1 | 2 |
| Stomach— | | |
| Hemorrhagic areas | 2 | 1 |
| Petechiae | 2 | .. |
| Duodenum— | | |
| Hyperemia of mucosa | 2 | .. |
| Petechiae | 1 | .. |
| Ulcers | 1 | .. |
| Ileum— | | |
| Petechiae | 2 | .. |
| Ulcers | .. | 1 |
| Colon— | | |
| Petechiae | 5 | 2 |
| Intussusception | .. | 1 |
| Marked subcutaneous fat | .. | 2 |

Ascarides were present in the intestines in three cases in which petechiae were found, and were also present in two cases in which no petechiae were found.

Experiment.—A four-months-old puppy without a jacket was kept in the incubator for one month at a mean temperature of 35.9° C. and a mean humidity of 72.5 per cent. A control puppy of the same litter was kept in the room, the mean temperature of which was about 25° C. The animal in the incubator thrived, increasing in weight from 2,020 gm. to 3,390 gm., while the control puppy increased from 1,920 gm. to 2,520 gm. The rectal temperature of the incubator animal was about 1 degree Centigrade higher than that of the control. The latter developed a diarrhea, which doubtless influenced his weight curve.

Experiment.—In the latter part of Experiment 6 a shaved puppy without a jacket was placed in the incubator, in addition to the usual jacketed and unjacketed animals. This shaved puppy seemed more comfortable than the others and his rectal temperature was usually about 0.4° C. lower than that of the unshaved, unjacketed incubator-control puppy.

DISCUSSION

The main means of heat loss in puppies under ordinary conditions are:

1. Radiation and conduction.
2. Evaporation of water.
 - (a) From the lungs and tongue.
 - (b) From the sweat glands of the paws.
 - (c) Through so-called insensible perspiration through the skin of the entire body.

At relatively low temperatures, conduction and radiation play the more important rôle with regard to heat loss. At high temperatures,

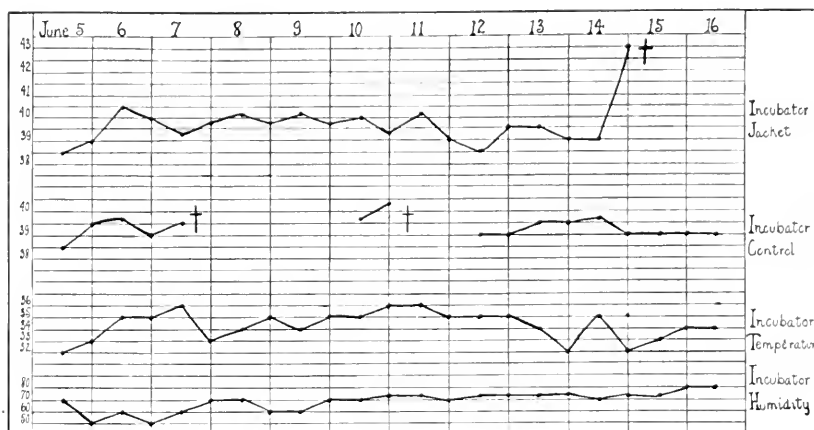


Fig. 5.—Experiment 5.

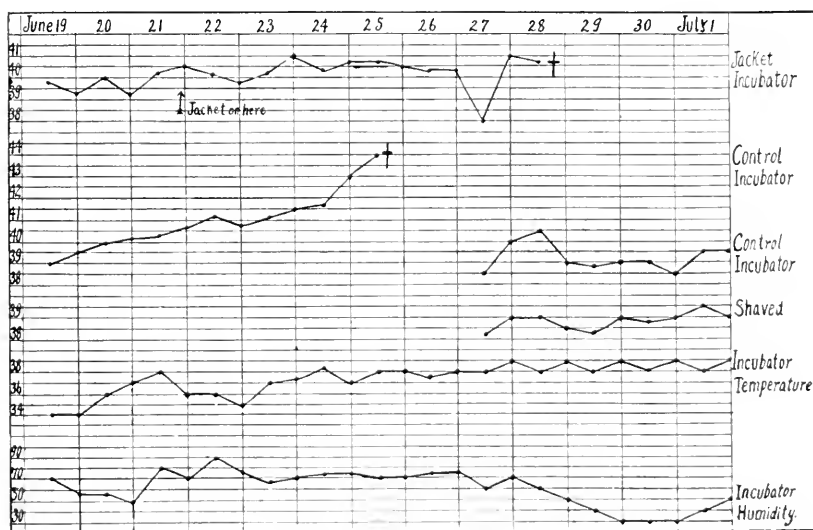


Fig. 6.—Experiment 6.

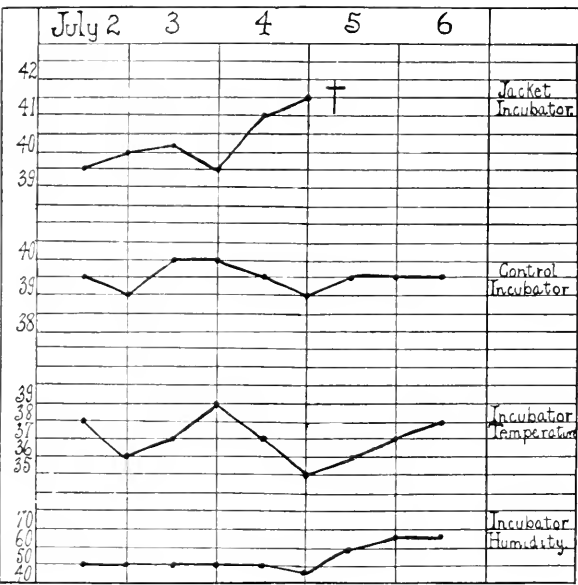


Fig. 7.—Experiment 7.

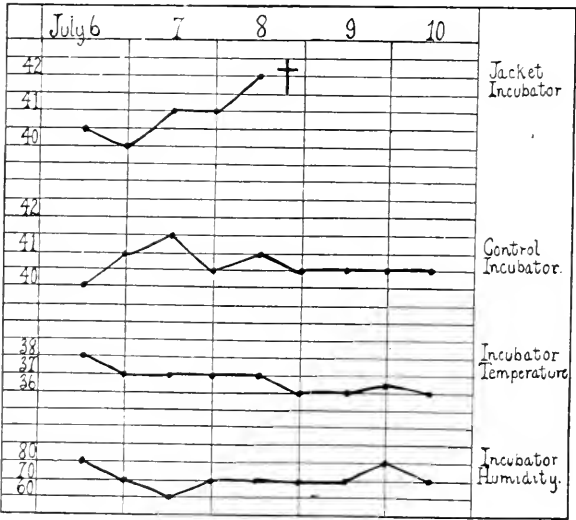


Fig. 8.—Experiment 8.

however, evaporation of water becomes more important. Since puppies perspire only on the paws (Luschsinger¹⁰), except under very unusual conditions,¹¹ panting becomes very important at high temperatures in increasing the heat loss by evaporation of water from the lungs and tongue. In our experiments, the jackets interfere only with heat loss through conduction and radiation, and the evaporation of the so-called insensible perspiration. In spite of this, i. e., without influencing appreciably the mechanism of heat loss, most important at high temperatures (evaporation), the interference with the less important factors at high temperatures (radiation and conduction) led to deleterious results.

Clothing interferes with heat loss by conduction, radiation and possibly evaporation of insensible perspiration in the infant as well as in the puppy. While conduction and radiation become less important as a means of heat loss, as the surrounding temperature approaches that of the body, one may deduct by analogy (cf. our experiments) that this relatively slight inhibition of heat loss may suffice to induce untoward results. In addition some infants, at least, perspire from the sweat glands of the body in general at high temperatures, and the clothing in such cases, if not freely permeable, may also interfere with heat loss by evaporation.

A portion of the infant deaths, especially those occurring in the first hot days of summer, is probably due to heat stasis per se (Finkelstein,¹² Rietschel,⁶ Liefmann and Lindemann,⁸ L. F. Meyer,¹³ etc.). It seems probable to us that there are many more cases in which disturbed heat regulation, though not sufficient to produce death, suffices to cause disturbances in the body functions, especially those of the digestive tract. The following case, reported by Wolff,¹⁴ seems to support this view:

A 2-months-old infant prematurely born (seventh month), came into the hospital suffering with a diarrhea. The infant was put into an incubator, the food regulated and the condition soon cleared up. Later, the child was removed to a crib and surrounded by hot-water bottles. One day, by accident, the temperature of the water in the bottles was too high and within a few hours the child developed a diarrhea with frequent green liquid defecations and vomiting. The fontanel became sunken, the child became semicomatose, the temperature rose to 42 C., and the clinical picture was that of Finkelstein's alimentary

10. Luschsinger: Cf. Hermann's *Handbuch der Physiologie*, Leipzig, 1883, p. 427.

11. Goltz and Ewald (*Pflüger's Arch. f. d. ges. Physiol.*, 1896, lxiii, 370), say that after the dog's cervical cord had been cut and the animal was held in the incubator, there soon became noticeable a layer of perspiration over the entire haired surface of the body excepting the head. The animal was not overheated, for there was neither tachypnea nor tachycardia.

12. Finkelstein: *Ueber den Sommergipfel der Säuglingssterblichkeit*, Deutsch. med. Wchnschr., 1909, xxxii.

13. Meyer, L. F.: *Die Morbidität und Mortalität der Säuglinge im Sommer*, 1911. *Deutsch. Naturforsch. u. Aertzte*, 1911, Wiesbaden, 1912, xxvii, 55.

14. Wolff: *Beitrag zur Frage der Sommersterblichkeit der Säuglinge*, *Jahrb. f. Kinderh.*, 1913, lxxvii, 569.

intoxication. On removal of the external heat and after giving a bath, but without any other change whatsoever, the infant's condition returned to normal in a very short time.

In a majority of cases of intestinal disturbance caused by a disturbed heat equilibrium, therapeutic results cannot be expected of measures intended to increase heat loss. The damage done to the infant organism is already too great. Results are, however, to be expected from prophylactic measures. Rubner¹ has shown that in adults, with food, health and clothing at an optimum, comfort is experienced with the surrounding temperature of 16 to 25 C. In the adult, clothing is almost automatically adjusted to the feeling of comfort; whereas in the infant, where the question of clothing is even more important because of the relatively much greater surface area, this regulation must depend on the judgment or whim of the caretaker. Sleeplessness, restlessness, and increased irritability are signs of discomfort in the infant that is overclothed. We are gathering statistics, to be published later, which thus far show surprisingly little difference between the weights of indoor clothing commonly worn by infants during the summer and winter.

Infected food as an element in summer mortality of infants, once considered the prime factor, has within the past few years been given a secondary place by many investigators. This change in view has probably come about principally because of the fact that where good milk has been furnished as the only food, less attention being paid to the other factors, the death rate has been disappointingly little influenced (Thiemich,¹⁵ Keller,¹⁶ Liefmann,¹⁷ Rietschel,¹⁸ etc.).

SUGGESTIONS

In considering what steps may be taken to prevent or reduce the high summer death rate of infants, we believe that a number of factors must be adjusted:

1. Decrease heat production by giving less food, more suitable food and more water.
2. Increase heat elimination by less and more permeable clothing, better circulation of air and frequent baths.
3. Guard against infection (through food and otherwise).

We wish to express our thanks to Mrs. Henry F. Helmholtz for her kind assistance in preparing the charts.

15. Thiemich: Die Sozialen Beziehungen und Aufgaben der Kinderheilkunde, Deutsch. med. Wchnschr., 1913, xxxix, 1739.

16. Keller, A.: Der Stand der Säuglingsfürsorge. Stenogr. Ber. u. d. Verhandl. d. Deutsch. Kong. f. Säuglingsschutz, Berlin, 1907, p. 27.

17. Liefmann: Die Bedeutung sozialer Momente für die Säuglingssterblichkeit, Ztschr. f. Hyg., 1909, lxii, 199.

18. Rietschel: Sommerhitze, Wohnungstemperatur und Säuglingssterblichkeit, Ztschr. f. Kinderh., 1911, i, 546; Zur Aetiologie des Sommer brechdurchfalls der Säuglinge, Monatschr. f. Kinderh., 1911, ix, 39.

PROTOCOLS

TABLE 2.—DATA OBTAINED IN EXPERIMENT 1

| Date | Hour | Incubator Puppies | | Outside Control Puppy | Incubator Temperature | Incubator Humidity Per Cent. | Room Temp. |
|--------|---------|--------------------|-------------------|-----------------------|-----------------------|------------------------------|------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | Temp. °C. | | | |
| May 20 | 4 p. m. | 39.5 | 39.5 | 38.2 | 37 | 50 | 28.3 |
| May 21 | 8 a. m. | 40. | 38.5 | 38.6 | 34 | 70 | |
| | 4 p. m. | 40.5 | 39.5 | 39.6 | 35 | 70 | 24.4 |
| May 22 | 8 a. m. |* | 38.5 | 38.8 | 35 | 70 | |
| | 4 p. m. | ... | 39. | 39.4 | 35 | 70 | 31.1 |

* Found dead.

The outside control animal had no jacket on in Experiment 1. The jacket of the incubator puppy was wrapped with a thin layer of plaster-of-Paris gauze (instead of adhesive plaster as in Experiments 2, 4, 5, 6, 7, 8). The weight of jacket = 90 gm. Stools of all puppies practically normal.

Post mortem on jacketed incubator puppy:

Skull: Meninges somewhat injected, cortical vessels prominent.

Abdominal Cavity: Peritoneal surfaces smooth, moist, shiny.

Pleural Cavity: Surfaces smooth, moist, shiny.

Pericardial Cavity: Normal.

Heart: No thrombi, no hemorrhages.

Lungs: Marked hyperemia, no consolidation, crepitation throughout.

Thymus: Pale pink, eight to ten pinhead sized hemorrhages just beneath the surface.

Spleen, liver, pancreas, kidneys and bladder appear normal.

Stomach: Distended with gas, contains coagulated milk, mucosa pale.

Intestines: Somewhat distended, mucosa of small intestines pale pink.

Colon and Rectum: Somewhat hyperemic. There are from forty to fifty pinhead-sized hemorrhages in the mucosa and a few streaks of free blood on the mucosa of the rectum. Eight ascarides in the small intestine.

TABLE 3.—DATA OBTAINED IN EXPERIMENT 2

| Date | Hour | Incubator Puppies | | Outside Control Puppy | Incubator Temperature °C. | Incubator Humidity Per Cent. | Room Temp. |
|--------|---------|--------------------|-------------------|-----------------------|---------------------------|------------------------------|------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | (Jacketed) Temp. °C. | | | |
| May 25 | 4 p. m. | 39.2 | 38.2 | 38.2 | 29 | 50 | 23.3 |
| May 26 | 8 a. m. | 39.5 | 38.8 | 39.0 | 28 | 50 | 23.9 |
| | 4 p. m. | 39.0 | 39.0 | 39.2 | 32 | 50 | 23.3 |
| May 27 | 8 a. m. | 39.5 | 38.8 | 39.0 | 36 | 50 | 23.3 |
| | 4 p. m. | 39.8 | 39.2 | 38.4 | 34 | 50 | 23.3 |
| May 28 | 8 a. m. | 39.8 | 39.7 | 38.4 | 34 | 50 | 27.2 |
| | 4 p. m. | 40.0 | 38.8 | 38.2 | 37 | 50 | 27.2 |
| May 29 | 8 a. m. |* | 39.5 | 39.1 | 34 | 50 | 30.5 |
| | 4 p. m. | | 39.0 | 39.0 | 37 | 50 | 28.9 |

* Found dead.

Jackets in Experiment 2 were made of a layer of cotton between gauze and covered with a layer of flannel. Weight of jacket = 70 gm. Stools were slightly loose; the outside control had mucus in the stools and once there was a tinge of blood.

Post mortem on the jacketed incubator puppy:

Skull: Meninges injected; cortical vessels prominent.

Abdominal, pleural and pericardial cavity surfaces normal.

Heart: Normal (no thrombi, no hemorrhages).

Lungs: Marked hyperemia, no consolidation, excess of blood-stained fluid expressed on incision.

Thymus: Pale pink, a number of pinhead-sized hemorrhages just below surface in center of lobules.

Spleen, liver, pancreas, kidneys, bladder and adrenals appear normal.

Stomach: Two hemorrhagic areas the size of a dime. No ulcers.

Duodenum: Mucosa pink, no hemorrhages.

Jejunum and ileum normal.

Colon and Rectum: A few small hemorrhagic areas; streaks of blood on the mucosa. No ulcers seen.

TABLE 4.—DATA OBTAINED IN EXPERIMENT 3

| Date | Hour | Incubator Puppies | | Outside Control Puppy Temp. °C. | Incubator Temp. ° C. | Incubator Humidity Per Cent. | Room Temp. ° C. |
|--------|---------|-----------------------|----------------------|--|----------------------------|---------------------------------------|-----------------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | | | | |
| May 30 | 4 p. m. | 38.0 | 40.0 | 39.0 | 34 | 50 | 21.7 |
| May 31 | 8 a. m. | 39.0 | 39.0 | 38.6 | 29 | 50 | 24.4 |
| | 4 p. m. | 39.5 | 38.5 | 38.4 | 33 | 60 | 23.9 |
| June 1 | 8 a. m. | 40.0 | 39.5 | 39.2 | 30 | 70 | 24.4 |
| | 4 p. m. |* | 39.5 | 39.4 | 32 | 60 | 25.5 |

* Found dead.

The jackets consisted of two layers of canton flannel and one layer of adhesive plaster. Jacket of the incubator animal = 60 gm. The animal was found dead under the incubator basket.

Postmortem on incubator (jacketed) puppy:

Skull: Meninges and cortical vessels slightly injected.

Abdominal, pleural and pericardial cavity surfaces normal.

Heart: Normal.

Lungs: Marked hyperemia, somewhat firm in some parts, but no pneumonic areas.

Thymus: Small petechial hemorrhages just beneath the surface in the center of the lobules.

Spleen, liver, pancreas and bladder appear normal.

Stomach: Normal. Small Intestine: Normal. Colon and Rectum: A number of small hemorrhages in the mucosa. No ascarides.

TABLE 5.—DATA IN EXPERIMENT 4

| Date | Hour | Incubator Puppies | | Outside Control Puppy Temp. °C. | Incubator Temp. ° C. | Incubator Humidity Per Cent. | Room Temp. ° C. |
|--------|---------|-----------------------|----------------------|--|----------------------------|---------------------------------------|-----------------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | | | | |
| June 2 | 4 p. m. | 41.0 | 39.5 | 39.4 | 35 | 50 | 23.3 |
| June 3 | 8 a. m. | 40.0 | 39.5 | 39.2 | 35 | 50 | 23.3 |
| | 4 p. m. | 42.0 | 38.5 | 39.0 | 35 | 50 | 25.5 |
| June 4 | 8 a. m. | 41.5 | 38.5 | 38.6 | 35 | 50 | 23.3 |
| | 4 p. m. | 43.0 | 40.0 | 39.4 | 37 | 50 | 27.8 |
| June 5 | 8 a. m. |* | 38.5 | 38.2 | 31 | 60 | 27.8 |
| | 4 p. m. | | 38.5 | 38.0 | 32 | 60 | 28.9 |

* Found dead.

The jackets were as described in Experiment 3. The incubator animals developed a diarrhea; the last few stools of the jacketed puppy contained mucus and blood.

Post mortem on jacketed incubator puppy:

Skull: Meninges and cortical vessels slightly injected.

Abdominal, pleural and pericardial cavity surfaces normal.

Heart: Normal.

Spleen, pancreas, liver, kidneys and bladder appear normal.

Stomach: Mucosa pale.

Duodenum: Mucosa hyperemic.

Jejunum and Ileum: Normal. Colon and Rectum: Small hemorrhages in mucosa. No ascarides.

TABLE 6.—DATA OBTAINED IN EXPERIMENT 5

| Date | Hour | Incubator Puppies | | Outside Control Puppy Temp. °C. | Incubator Temp. ° C. | Incubator Humidity Per Cent. | Room Temp ° C. |
|---------|---------|-----------------------|----------------------|---------------------------------------|----------------------------|---------------------------------------|----------------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | | | | |
| June 6 | 8 a. m. | 39.0 | 39.5 | 38.5 | 33 | 50 | 23.9 |
| | 4 p. m. | 40.5 | 39.8 | 38.2 | 35 | 60 | 23.9 |
| June 7 | 8 a. m. | 40.0 | 39.0 | 38.4 | 35 | 50 | 23.3 |
| | 4 p. m. | 39.2 | 39.5 | 38.6 | 36 | 60 | 23.3 |
| June 8 | 8 a. m. | 39.8 |* | 38.2 | 33 | 70 | 24.4 |
| | 4 p. m. | 40.2 | | 38.4 | 34 | 70 | 23.3 |
| June 9 | 8 a. m. | 39.8 | | 39.0 | 35 | 60 | 23.3 |
| | 4 p. m. | 40.4 | | 39.2 | 34 | 60 | 23.3 |
| June 10 | 8 a. m. | 39.6 | 39.8 | 39.2 | 35 | 70 | 21.1 |
| | 4 p. m. | 40.0 | 40.4 | 39.4 | 35 | 70 | 22.2 |
| June 11 | 8 a. m. | 39.2 |* | 38.2 | 36 | 72 | 23.3 |
| | 4 p. m. | 40.2 | | 39.0 | 36 | 72 | 21.1 |
| June 12 | 8 a. m. | 39.0 | | | 35 | 70 | |
| | 4 p. m. | 38.5 | 39.0 | | 35 | 75 | 23.9 |
| June 13 | 8 a. m. | 39.5 | 39.0 | | 35 | 75 | 24.4 |
| | 4 p. m. | 39.5 | 39.5 | | 34 | 75 | 23.3 |
| June 14 | 8 a. m. | 39.0 | 39.5 | | 32 | 75 | 23.3 |
| | 4 p. m. | 39.0 | 39.8 | | 35 | 70 | 23.3 |
| June 15 | 8 a. m. | 43.0 | 39.0 | | 32 | 75 | |
| | 4 p. m. |* | 39.0 | | 33 | 75 | 23.9 |
| June 16 | 8 a. m. | | 39.0 | | 34 | 80 | |
| | 4 p. m. | | 39.0 | | 34 | 80 | 23.9 |

* Found dead.

The jackets were as in Experiment 3. The stools of the incubator animals were, at times, thin and yellow, with mucus occasionally. The first control animal in the incubator was exceptionally fat, and the second incubator control animal appeared sick a few hours after being put into the incubator.

Necropsy on the jacketed incubator puppy:

Skull: Meninges and cortical vessels hyperemic.

Abdominal, pleural and pericardial cavity surfaces normal

Heart: Normal.

Lungs: Nearly collapsed, congestion and bogginess of the lower lobes, bronchi normal.

Thymus: Exceptionally small. No hemorrhages.

Spleen, pancreas, liver, kidneys and bladder appear normal, except for a slight hyperemia of the papillae of the kidneys.

Stomach: Mucosa hemorrhagic in pyloric region.

Duodenum, jejunum and ileum slight hyperemia of mucosa.

Colon and Rectum: More marked hyperemia.

Necropsy on first incubator control puppy of Experiment 5:

Skull: Meningeal and cortical vessels injected.

Abdomen: Much distended with gas.

Subcutaneous Tissues: Emphysematous; marked adiposity.

Abdominal, pleural and pericardial cavity surfaces normal.

Peritoneal Cavity: The contents of the stomach and three ascarides were found in the peritoneal cavity (probably post mortem).

Thymus: Many hemorrhagic spots beneath the surface, in the center of the lobules.

Heart: Anemic; otherwise normal.

Lungs: Hyperemic.

Spleen, pancreas, kidneys and bladder normal. Liver soft; some post mortem changes.

Stomach: There is a 5 cm. tear in the fundus region, from which the gastric contents escaped into the peritoneal cavity.

Intestines: Show post mortem changes and are very much distended with gas.

Post mortem on second incubator control puppy:

Skull: Not opened.

Peritoneal, pleural and pericardial cavity surfaces normal except for a slight congestion of the pleural surfaces.

Heart: In systole; a few petechial hemorrhages under the epicardium; myocardium is pale.

Thymus: Numerous hemorrhagic areas (flaxseed size) under the surface in the center of lobules.

Spleen and liver congested and friable. Kidneys pale. Bladder and adrenals are normal.

Stomach: The mucosa is pale.

Small Intestine: Mucosa is pale.

Colon: Mucosa is pale.

Rectum: Many small hemorrhages in the mucosa.

Five ascarides in the ileum and colon.

TABLE 7.—DATA OBTAINED IN EXPERIMENT 6

| Date | Hour | Incubator Puppies | | Outside Control (Jacketed) Temp. °C. | Incubator Temp. ° C. | Incubator Humidity Per Cent. | Room Temp. ° C. |
|---------|---------|-------------------|---------------|--|----------------------------|---------------------------------------|-----------------------|
| | | Temp. ° C. | Temp. ° C. | | | | |
| June 19 | 4 p. m. | 39.8 | 39.0 | 38.8 | 34 | 70 | 23.3 |
| June 20 | 8 a. m. | 39.3 | 39.5 | 38.6 | 34 | 58 | 23.3 |
| | 4 p. m. | 40.0 | 40.0 | 38.4 | 35 | 58 | 23.3 |
| June 21 | 8 a. m. | 39.3 | 40.3 | 38.4 | 36 | 50 | 23.3 |
| | 4 p. m. | 40.2 | 40.3 | 38.6 | 37 | 80 | 24.4 |
| | | Jacket on here | Control | | | | |
| June 22 | 8 a. m. | 40.5 | 40.7 | 38.6 | 35 | 70 | 23.9 |
| | 4 p. m. | 40.3 | 41.1 | 38.8 | 35 | 90 | 26.1 |
| June 23 | 8 a. m. | 39.8 | 40.8 | 38.4 | 34 | 78 | 25.0 |
| | 4 p. m. | 40.3 | 41.3 | 38.9 | 36 | 70 | 26.7 |
| June 24 | 8 a. m. | 41.0 | 41.5 | 38.6 | 36.5 | 70 | 26.7 |
| | 4 p. m. | 40.3 | 41.7 | 38.6 | 37.6 | 77 | 24.3 |
| June 25 | 8 a. m. | 40.7 | 43.0 | 38.8 | 36 | 77 | 23.3 |
| | 4 p. m. | 40.7 | 44.0 | 38.2 | 37 | 70 | 23.3 |
| June 26 | 8 a. m. | 40.5 |* | 38.4 | 37 | 70 | 23.3 |
| | 4 p. m. | 40.3 | | 38.6 | 36.6 | 75 | 23.3 |

TABLE 7.—(Continued)

| Date | Hour | Incubator Puppies | | Outside Control (Jacketed) Temp. °C. | Incubator Temp. °C. | Incubator Humidity Per Cent. | Room Temp. °C. |
|---------|---------|-------------------|----------------|--|---------------------------|---------------------------------------|----------------------|
| | | Temp. °C. | Temp. °C. | | | | |
| | | | New control | Shaved incubator puppy | | | |
| June 27 | 4 p. m. | 38.0 | 38.5 | 38.3 | 37 | 70 | |
| June 28 | 8 a. m. | 41.0 | 40.0 | 39.0 | 37 | 55 | |
| | 4 p. m. | 40.7 | 40.5 | 39.0 | 38 | 40 | |
| June 29 | 8 a. m. |* | 39.0 | 38.5 | 37 | 38 | |
| | 4 p. m. | | 38.8 | 38.4 | 38 | 30 | |
| June 30 | 8 a. m. | | 39.0 | 39.0 | 37 | 30 | |
| | 4 p. m. | | 39.0 | 38.8 | 38 | 40 | |
| July 1 | 8 a. m. | | 38.5 | 39.0 | 37 | 50 | |

* Found dead.

In Experiment 6 neither incubator puppy had a jacket for the first three days; on the fourth day the usual jacket was put on one of the animals. The control died seven days after being put into the incubator. Blood was found in this animal's stools a few hours before death (intussusception; see notes below). The jacketed incubator animal died two days later. In the latter part of this experiment three animals were in the incubator: one shaved, one with a jacket and the normal control. The shaved animal showed less distress than the other two. The first incubator control puppy and the jacketed incubator puppy had watery stools part of the time; the second control puppy and the shaved puppy had normal stools.

Post mortem on jacketed incubator puppy of Experiment 6:

Skull: Meningeal and cortical vessels injected.

Peritoneal, pleural and pericardial cavity surfaces normal.

Heart: Normal.

Lungs: Mottled purple areas, the rest of the lungs somewhat hyperemic.

Thymus: Petechial hemorrhages beneath the surface in the center of the lobules.

Spleen, pancreas, liver and bladder normal.

Kidneys: Hyperemia of the papillae.

Stomach: A few hemorrhagic spots near the pylorus.

Duodenum: A few small ulcers, one about the size of a flaxseed.

Jejunum: Normal. Ileum: There are a few petechiae in the lower part.

Colon: There are about twenty petechiae in the cecal region; no macroscopic ulcers.

Post mortem on first control incubator puppy of Experiment 6:

Marked adiposity.

Skull: Meninges and cortical vessels are injected.

Peritoneal, pleural and pericardial cavity surfaces normal.

Heart: Normal.

Lungs: Congestion of the lower lobes; no consolidation.

Thymus: There are about twelve petechiae just beneath the surface. Spleen congested.

Pancreas, liver, kidneys and bladder normal.

Stomach: A few petechiae in the mucosa.

Ileum: A few pinhead-sized ulcers. Colon: An intussusception, about 5 cm. long involves the cecum and ascending colon. The lumen is patent for a small sound. The intussusception is easily reduced; the mucosa there is somewhat necrotic. The visceral peritoneum is smooth and shiny. An edematous dark red area is found about 5 cm. from the intussusception. The appendix is edematous with a marked injection of its mucosa.

TABLE 8.—DATA OBTAINED IN EXPERIMENT 7

| Date | Hour | Incubator Puppies | | Outside Control Puppy Temp. °C. | Incubator Temp. °C. | Incubator Humidity Per Cent. |
|--------|---------|-----------------------|----------------------|--|------------------------|------------------------------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | | | |
| July 2 | 8 a. m. | | 39.5 | 39.0 | 38 | 50 |
| | 4 p. m. | 39.5 | 39.5 | 38.8 | 38 | 50 |
| July 3 | 8 a. m. | 40.0 | 39.0 | 38.5 | 36 | 52 |
| | 4 p. m. | 40.3 | 40.0 | 39.5 | 37 | 50 |
| July 4 | 8 a. m. | 39.5 | 40.0 | 39.0 | 39 | 50 |
| | 4 p. m. | 41.0 | 39.5 | 40.0 | 37 | 47 |
| July 5 | 8 a. m. | 42.0 | 39.0 | 39.8 | 35 | 60 |
| | 4 p. m. |* | 39.8 | 38.5 | 36 | 70 |
| July 6 | 8 a. m. | | 39.8 | 39.5 | 37 | 68 |

* Found dead.

The stools of the jacketed incubator puppy were loose at times, with, occasionally, particles of mucus. The stools of the control puppies were normal. Jackets as in Experiment 3.

Post mortem on jacketed incubator puppy of Experiment 7:

Skull: Not opened.

Peritoneal, pleural and pericardial cavity surfaces normal.

Heart: There are three lintel sized hemorrhages beneath the epicardium.

Lungs: There is some congestion of the lower lobes.

Thymus: A number of small petechiae just beneath the surface.

Spleen, liver, pancreas, kidneys, adrenals and bladder normal.

Small Intestine: Excessive mucus with edema of the mucosa. Three ascarides in the small intestine.

Colon: Serosa hyperemic; mucosa normal.

TABLE 9.—DATA OBTAINED IN EXPERIMENT 8

| Date | Hour | Incubator Puppies | | Incubator Temp. °C. | Incubator Humidity Per Cent. |
|---------|---------|-----------------------|----------------------|------------------------|------------------------------------|
| | | Temp. °C. Jacketed | Temp. °C. Control | | |
| July 6 | 4 p. m. | 40.5 | 40.0 | 38 | 80 |
| July 7 | 8 a. m. | 40.0 | 41.0 | 37 | 70 |
| | 4 p. m. | 41.0 | 41.5 | 37 | 60 |
| July 8 | 8 a. m. | 41.0 | 40.5 | 37 | 70 |
| | 4 p. m. | 42.0 | 41.0 | 37 | 75 |
| July 9 | 8 a. m. |* | 40.5 | 36 | 75 |
| | 4 p. m. | | 40.5 | 36 | 75 |
| July 10 | 8 a. m. | | 40.5 | 36.5 | 80 |
| | 4 p. m. | | 40.5 | 36 | 70 |

* Found dead.

Jacket as in Experiment 3.

Post mortem on jacketed incubator puppy of Experiment 8:

Skull: Meningeal and cortical vessels of the left hemisphere injected; those of the right anemic, with a marked edema of the brain.

Peritoneal, pleural and pericardial cavity surfaces normal.

Heart: Small and anemic.

Lungs: Pale, crepitate throughout; lintel-sized deep red areas in the dependent portions.

Thymus: Five small petechiae just beneath the surface.

Spleen: Is hyperemic and soft.

Liver, pancreas, kidneys, adrenals and bladder normal.

Stomach: Contains bile-stained fluid; there are about 40-50 petechiae in the mucosa near the fundus.

Small Intestine: Three flaxseed-sized hemorrhages in the mucosa, no ulcers. Three ascarides in the small intestine.

Colon: Four small hemorrhagic areas in the lower part of the colon.

TUBERCULOUS TUMORS OF THE BRAIN

REPORT OF A CASE AND BRIEF SUMMARY OF THE LITERATURE*

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Tuberculous tumors are the most frequent of all cerebral tumors. During childhood they are especially common, forming over 50 per cent. of all brain tumors.⁴⁸ In 300 cases of brain tumor in persons under 18 years of age, reported by Starr,⁴⁵ 152 were tuberculous. Peterson³⁷ reports 335 cases of which 166 were tuberculous.

Brain tubercle is almost always secondary to some other tuberculous lesion. In about 25 per cent. of the cases it is multiple.⁴⁸

Tubercles are most commonly found in the cerebellum. The pons is also a rather frequent seat. Larger tubercles are comparatively infrequently found in the cortex; when found they are usually situated in the paracentral lobe.⁴⁸ The situation in Starr's⁴⁵ 152 cases was as follows: cerebellum 47, pons 19, corpora quadrigemina and crura 16, basal ganglia and lateral ventricles 14, cortex cerebri 13, centrum ovale 6, medulla 2.

The tubercle usually forms about a blood vessel, caseation occurring in the center. It is sharply defined from the surrounding brain substance, which undergoes softening.

The following case has many points of interest, and is therefore reported.

J. S., a colored boy of not quite 7, had been an inmate of the St. Elizabeth's Home for three years. Nothing was known of his history previous to his entrance into the institution. When first seen in June, 1912, the child was fairly well nourished, but pale and undersized. His intelligence was as good as that of the average child of his age in the institution. While in the home the child had not complained and had had no illness. The child had a convulsion in June, 1912, and it was said, passed a roundworm. A blood examination showed a marked eosinophilia. Santonin and calomel were given; he did not, however, pass any worms. Convulsions epileptiform in character occurred at rather irregular intervals. These convulsions always set in with a spasm of the right arm and leg. Just before the occurrence of a convulsion, the child would run up to the Sister and say, "Sister, I'm sick." A blood examination made some-

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what later did not show an eosinophilia. The Wassermann reaction was positive. The child showed general glandular enlargement, but nothing important was found on physical examination at this time. The patient was given active antisyphilitic treatment over a period of five months without any improvement. During the summer and autumn of 1912 the convulsions became more and more frequent, the child's appetite failed; he lost weight rapidly, became markedly emaciated and very weak. Toward the end of autumn the convulsions became very violent in character, always coming on with twitchings of right arm and leg. On Jan. 11, 1913, following a violent convulsion, the patient became acutely ill, the temperature rose, the respiration became rapid and labored. On physical examination, patches of crepitation were found over the whole right lung. Bronchial breathing was also noticed at various points. These pneumonic symptoms continued; the patient gradually became weaker and weaker. On the 21st the abdomen became rigid, distended, tender and dullness in the flanks indicated fluid. The child died Jan. 24, 1913, his illness having covered a period of from seven to eight months.

Jan. 24, 1913, at necropsy, the body was that of a markedly emaciated boy of about 7 years. The right lung was involved in an extensive caseous pneumonia and the pleurae were thickened and adherent over most of their surface. On section small and medium sized cavities could be seen in the upper lobe. The left pleurae were thickened and adherent over most of the lung, especially so near the apex. The left lung itself, with the exception of the apex, was free from tuberculosis. The bronchial lymph nodes were everywhere enlarged, some to the size of a walnut, quite dense and on section showed caseous centers. Microscopically, immense fibroid tubercles, some of which were hyaline and showed slightly caseous centers, were found in the left apex; they appeared to be inactive and to denote a very chronic course.

The heart showed no abnormalities.

The abdominal cavity contained a large quantity of yellowish turbid fluid and there were extensive peritoneal adhesions present binding coils of intestines to each other. Miliary tubercles were in evidence on the visceral peritoneum. The mesenteric nodes, both grossly and microscopically, showed extensive caseation.

The liver was large, and had the typical yellowish, waxy hue of a fatty liver. To the naked eye there was no evidence of tuberculosis, but microscopically small tuberculous foci with beginning caseation were found, mainly in the interlobular connective tissue but also intralobularly. The capsule showed a chronic inflammatory thickening with hyaline changes.

The spleen was slightly enlarged and congested, and near the hilum a small nodule about the size of a pea was found, which proved to be an accessory splenule. The capsule was thickened, and even to the naked eye showed fine pin head nodules of miliary tubercles. Hyaline changes in the trabeculae and in the blood vessel walls were found microscopically. The accessory splenule showed a few caseous and cellular foci and hyaline changes.

The kidneys on microscopical examination showed marked cloudy swelling and also fatty degeneration of the epithelium of the convoluted tubules and slight proliferative changes in some of the glomeruli, hyaline changes in the blood vessel walls, and inflammatory thickening of the capsule.

The pancreas showed no lesion of interest.

On running the fingers over the convexity of the brain, a number of hard shotlike elevations varying in size from a pea to a medium sized marble were felt in different portions of both cerebral hemispheres. The pia mater was everywhere congested, and over the areas just described appeared hazy and opaque, and was adherent. With these exceptions, the meninges were free from disease. On removal of the meninges and on closer examination, these areas were found to consist of dense white or grayish masses imbedded in the cerebral hemispheres. They apparently had little connection with the surrounding brain tissue, for they could be shelled out very easily.

Their exact location and size are indicated on the diagrams. The left cerebral hemisphere contained a number of conglomerate foci, forming a large mass situated in the ascending parietal and partly in the superior marginal and superior parietal convolutions opposite the leg, trunk and arm motor areas. As shown in the drawing (Fig. 1 *a*) the mass appeared on the surface and involved the gray matter in its upper part only, while the white matter beneath was involved to a greater extent, impinging on the gyri within the rolandic fissure.

The right cerebral hemisphere contained four masses of various dimensions, three of which were apparent on the external surface of

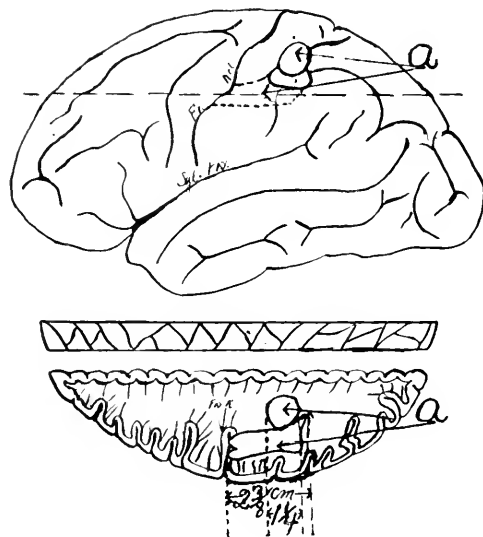


Fig. 1.—Left cerebral hemisphere: *a*, fused mass, maximum depth $2\frac{7}{8}$ cm., width $23\frac{1}{4}$ cm., length $23\frac{3}{8}$ cm.; dotted lines in upper drawing indicate where tumor passes beneath gray matter at about an angle of 10 degrees both anteriorly and externally. The diagrams in this and Figure 2 were drawn directly from the specimen, after the method employed by draftsmen in drawing a plan of an object. The disconnected horizontal lines passing across the cerebral hemisphere indicate the planes of section, which below are projected, the horizontal surfaces thus exposed, and at times the perpendicular edges of the corresponding sections.

the brain; the fourth, the largest, appeared only on section. As seen in the drawing (Fig. 2 *a*) one of these occupied the upper part of the midfrontal convolution and was well forward; another (Fig. 2 *b*) the lower part of the external surface of the occipital lobe (mid-occipital convolution); and a third (Fig. 2 *c*) was situated about the parieto-occipital sulcus, both on the external and mesial surfaces. The fourth mass (Fig. 2 *d*) was of large dimensions, conical in shape, its base involving the temporal operculum and extending across the limiting sulcus, involved also the upper part of the insula, the claustrum and

external capsule. Its tapering extremity passed upward lying posterior to the fissure of Rolando and between it and the sylvian fissure.

These masses could easily be seen to be made up of a number of conglomerate foci, fused together. On the whole, they were dense yellowish-white or grayish in color, and generally showed some caseation within the center. Histologically they showed the ordinary changes produced by the tubercle bacillus. An extensive caseous center

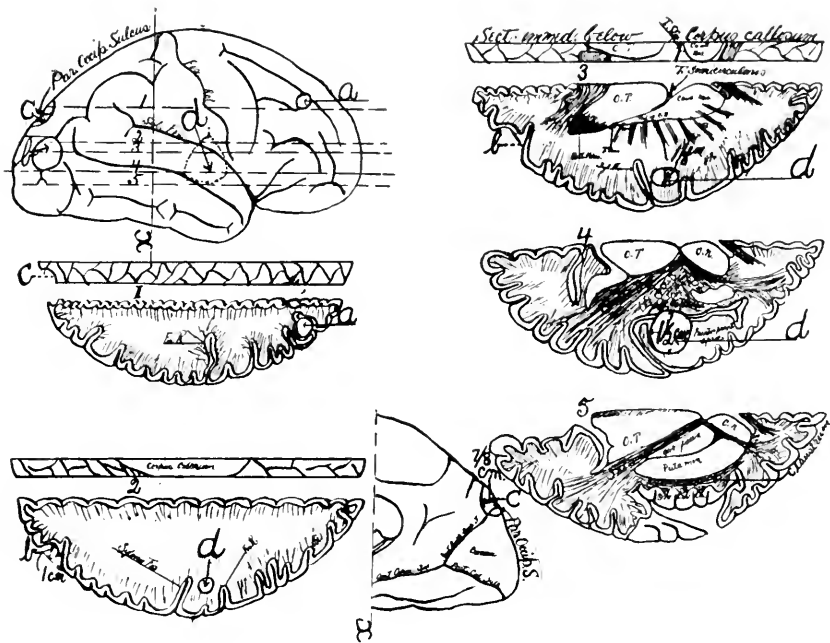


Fig. 2.—Right cerebral hemisphere: *a*, mass, diameter $3\frac{1}{4}$ cm., depth 1 cm.; *b*, mass, diameter $1\frac{1}{4}$ cm., depth 1 cm.; *c*, mass, diameter $1\frac{3}{8}$ cm., depth $\frac{1}{2}$ cm.; *d*, mass (appears in dotted lines in lateral view of cerebral hemisphere), from base to apex $3\frac{1}{4}$ cm., diameter of base $1\frac{1}{2}$ cm. In the fourth cross sectional view, the base of this mass is shown occupying the fronto-parietal operculum crossing the limiting sulcus of Reil, and invading the insula. The claustrum cannot be made out here with the naked eye. The fifth cross sectional view is below the level of the mass (*d*) and shows the normal relation of the parts.

The central figure below represents the mesial surface of Figure 2 posterior to line *x*.

was generally present, surrounded by a more cellular periphery and in some instances by a small margin of brain substance, which showed reactive inflammation.

The presence of numerous medium sized blood vessels in various stages of the pathological process was noticed. In the center of the nodules, the vessel-walls were extensively involved in the caseous process and contained necrotic and caseous thrombi. At the periphery

in the areas less involved the vessel-walls showed periarteritis and endarteritis and hyaline changes, and most of them also contained necrotic thrombi. Immediately surrounding the necrotic zone, epithelioid cells, partly degenerated, were found in large numbers. These in turn were surrounded by an area of reactive inflammation presenting perivascular round cell infiltration, with numerous plasma cells, round cells, variously shaped endothelial cells, and marked vascular congestion. The tuberculous giant cell with one or two exceptions was not found. The pia mater was caseous directly over the nodules, while immediately surrounding these areas, it showed merely a mild reactive inflammation. The rest of the pia mater over the brain was practically free from disease. Sections stained for tubercle bacilli showed them in great abundance. Innumerable tubercle bacilli abounded in and about the walls of several medium sized blood vessels. The arterial walls themselves had undergone hyaline degeneration, and endarteritis and periarteritis were present. The bacilli were so numerous and occurred in such large clumps that they could easily be recognized (Fig. 3 as red masses in the walls and for some distance about the blood vessels. With the oil-immersion lens, the individual bacilli could easily be seen making up these clumps; in a number of places they were found, within the lumen of the blood vessel, among the red blood cells (Fig. 4). They were also found with ease, scattered about caseous and inflammatory areas, occurring singly or in clumps, but in much less abundance than about the blood vessels.

The presence of immense numbers of tubercle bacilli in and about a large blood vessel of a caseous bronchial lymph node was noted, although in sections of the lung and other tuberculous organs tubercle bacilli were found singly and with great difficulty.

In view of the double plus Wassermann, a careful search for the *Spirochæta pallida* was made in the various diseased organs, but with negative results.

Although careful search was made of the large blood vessels at the base of the brain both grossly and microscopically, no evidence of tuberculosis was found. Cultures from lung grown on Löffler's serum medium showed the *Streptococcus mucosus*. The streptococci appeared in diplococcus form surrounded by a large conspicuous capsule.

In the case reported by us, the original focus from which the infection spread was possibly a latent focus in the fibroid apex of the left lung or a bronchial lymph node. The infection was early carried to the brain. The twitchings of the right arm and leg are easily explained by the tumor in the left ascending parietal convolution.

A tuberculous pneumonia and a general miliary tuberculosis occurred as a terminal condition, as is shown by the pathological find-

ings and the tubercle bacilli in the blood. This is the usual termination, as seen in most of the cases reported in the literature. The case is a typical one of solitary tubercle, or tuberculoma of the brain. All sections of tissues for microscopic examination were fixed in 10 per cent. of the commercial formaldehyd and embedded in celloidin. The staining process employed to demonstrate the tubercle bacillus in the tissues

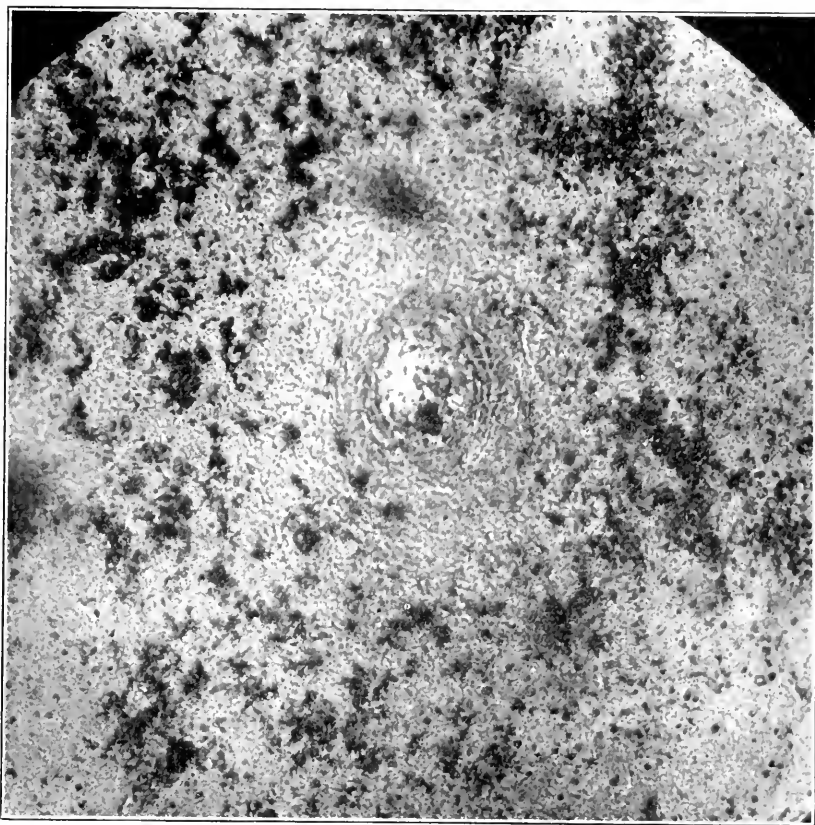


Fig. 3.—Photomicrograph of tuberculous nodule of brain, showing immense masses of tubercle bacilli surrounding arteriole and within its wall; $\times 103$.

was that of Kuhne's suitable for celloidin sections, but the Ziehl-Neelson-Gabbet method was also used. Levaditi's method for demonstrating the *Treponema pallidum* in tissues was employed.

Cases in which findings similar to those just described have been found are few. The following have been selected as typical.

Greive¹⁸ described a case of solitary tubercle in the right tegmentum, with degeneration in the fillet and superior peduncle of the cerebellum; occurring in a chronic tuberculous individual, male, aged 35, causing

paralysis of the right arm and leg. There were symptoms of brain tumor for nine months preceding death. Post mortem examination showed a chronic ulcerative tuberculosis of the lung, fatty liver and enlarged spleen. Examination of brain showed the meninges to be free from disease. The blood vessels in the right sylvian fissure showed extensive miliary and a few larger tubercles. The tumor in

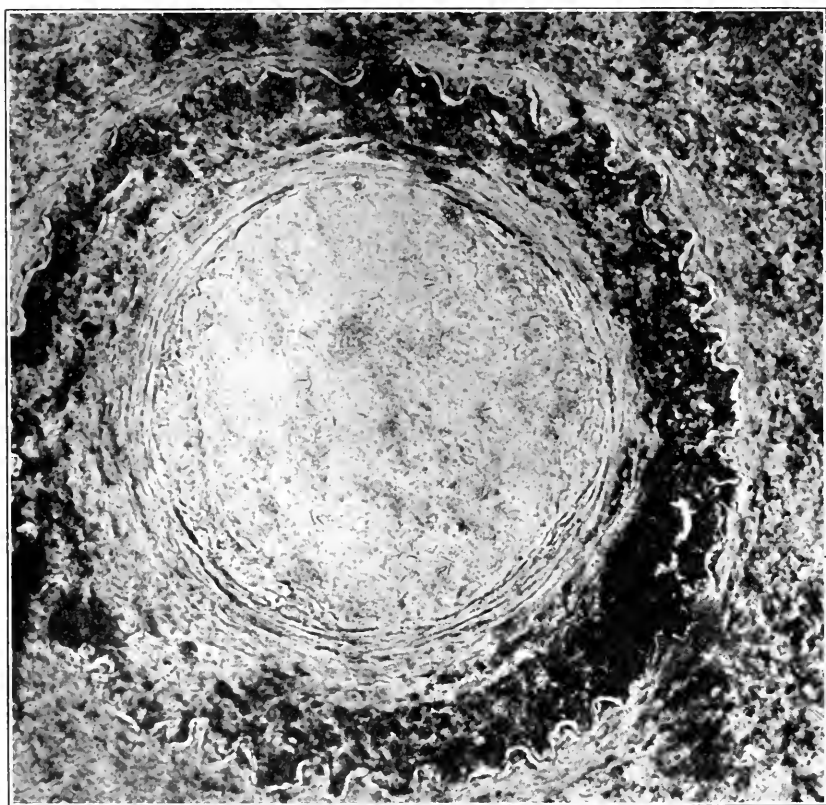


Fig. 4.—Photomicrograph of arteriole in tuberculous nodule of brain, showing endarteritis and tubercle bacilli within lumen; $\times 750$.

the right tegmentum was of hazelnut size, its largest diameter being about 1.7 cm.; it showed central softening and was apparently made up of an aggregation of smaller foci fused together. It could easily be shelled out. The microscopic description of the tumor is very similar to the one just described. The blood vessels were everywhere extensively involved in an endarteritis and periarteritis and the walls were definitely diseased. The condition found in a small artery in the periphery of the growth is of interest. Innumerable masses of tubercle bacilli were found in its thickened walls as well as in the

tissues for a short distance surrounding it, while in other parts of the mass very few if any bacilli could be found.

N. Dalton⁸ described a case of multiple tuberculous tumors of brain occurring in a child, 1 year of age. There were three tumors present, one in the pons, another at the back of the right internal capsule, and a third one in the cerebellum. There was no meningitis. Post mortem examination showed miliary tubercles present in nearly all organs. There was no history of tuberculosis or of syphilis in the family. The onset of symptoms followed a fall. There was paresis of both limbs and athetosis of the right arm. Otherwise no distinctive symptoms occurred. Death was apparently due to ulcerative stomatitis.

Renz³⁹ described a case of solitary tubercle of the left parietal lobe, the size of a billiard ball, occurring in an individual, 30 years of age. The patient was first seen with symptoms which pointed strongly to epilepsy. At that time tuberculous involvement of both apices of lungs was also found. With the exception of headache and vomiting, no new symptoms appeared. Post mortem examinations showed old healed tuberculous foci in both apices of the lungs, tuberculosis of right kidney and left suprarenal body, miliary tuberculosis of peritoneum covering the kidney and a solitary tubercle of left parietal lobe. The patient died at the end of one year.

J. L. Stevens⁴⁴ described a case of multiple tuberculous tumors in various parts of the brain, basal ganglia and cerebellum (from six to eight in all) occurring in a child 8 months old. The average size of the nodules was about that of a hazelnut. Clinically the symptoms were diverse and confusing "but in keeping with numerous tumors."

W. C. Chaffey⁷ reports a case in a child 2 years old with caseous tuberculous deposit in the floor of the fourth ventricle, $\frac{5}{8}$ by $\frac{3}{8}$ inch, and also smaller nodules about the size of an acorn in each lateral surface of the cerebellum and one in the upper anterior border of the right side of the pons. There were symptoms of tumor for four months previous to death, namely, left ptosis, paresis of the left side of the face; both lower extremities were very weak; the upper extremities were normal, and both knee jerks were increased. During life no tuberculous disease could be discovered anywhere. At necropsy both lungs were studded with fine miliary tubercles, the bronchial glands were tuberculous, as was also the lower part of the left kidney.

F. X. Dercum⁷ reported a large (7.5 cm. by 3.5 cm.) subcortical tuberculous tumor of the left occipital lobe, in a boy of 12 years of age, producing right sided hemiparesis and right homonymous hemianopsia, together with Wernicke's pupillary reaction as a distinct symptom. This tumor destroyed radiation of the optic thalamus, pressed

on the optic thalamus and corpora and probably caused slight pressure on the posterior limb of the capsule. Symptoms of tumor were present for at least one year preceding death.

J. S. Bristowe² reported several cases of tumors involving the parts in the neighborhood of the third and fourth ventricles and aqueduct of Sylvius, three of which are of the tuberculous type.

CASE 1.—Child, aged 7 years, tuberculous tumor, size of a marble, of the corpora quadrigemina followed by tuberculous meningitis, paralysis of both third nerves and ptosis and tremors of head, neck, arms and legs. No fits. Sickness and headache absent until end. No optic neuritis. On necropsy pleurae were found adherent, and gray tubercles were scattered on the lung; larger tubercles occurred in the spleen.

CASE 2.—Child aged 4 years. Tuberculous mass 1.5 cm. in diameter in third ventricle involving both thalami; also a smaller mass on internal surface of occipital lobe followed by tuberculous meningitis. Tremors and rigidity of arms and legs, drowsiness and irritability, optic neuritis and slight facial palsy were present. Convulsions, coma and elevation of temperature introduced a meningitis. No other tuberculous disease was found in the viscera, but patient had been operated on for scrofula of astragalus. Symptoms of tumor lasted for nine months.

CASE 3.—Child aged 4 years. Nine months' duration. No tuberculous disease found during life. Large tuberculous mass size of tangerine orange in left lobe of the cerebellum; another small mass imbedded in the gray matter of orbital surface of the frontal lobe. Effusions of fluid into ventricle, inability to walk, tremors of arms and head, optic neuritis, and blindness, frequent epileptiform attacks, headache, etc. No meningitis was present. Glands at root of lungs were caseous and there was a pyelitis of both kidneys; otherwise no other lesions were found.

The most interesting observations in the case reported by us are the great masses of tubercle bacilli found in the vessel-walls and within the caliber of the vessels in the tubercles in the brain and bronchial lymph nodes. The disintegration of the caseating thrombi would result in throwing great masses of tubercle bacilli into the circulation. We have been unable to find in the literature the report of any case of this condition in which tubercle bacilli were found within the blood vessel. The only cases in which tubercle bacilli are described as having been found in masses about the vessels and in the vessel walls is that of Greive.¹⁸ Our observation is therefore unique.

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THE AMMONIA AND UREA CONTENT OF INFANTS' STOOLS

WITH A DESCRIPTION OF METHODS *

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Since bacteria, like other living cells, require a certain intake of nitrogenous material for the maintenance of the chemical structure of their protoplasm, and many of them are also able to utilize it for their energy needs, it is evident that the mediums in which they grow must contain end products of their nitrogen metabolism. Steps in the utilization of protein by bacteria are not in the gross dissimilar from those of the same process in the complex animal organism. They hydrolyze protein, so far as we know, in exactly the same manner as do the digestive ferments and are able ultimately to split off ammonia from the products of hydrolysis just as this is accomplished somewhere in the body. It is very interesting that besides ammonia another familiar end product of protein metabolism—urea—has been measured in appreciable amounts in cultures of bacteria which are normal or occasional inhabitants of the lower intestinal tract.¹

The presence of ammonia in the stool may usually be demonstrated by adding water to a sample, making the mixture alkaline with potassium carbonate and then heating gently. The escaping ammonia may be detected by smelling, by the turning blue of a strip of moistened red litmus paper, or by noting the white deposit of ammonium chlorid on a glass rod which has been dipped in hydrochloric acid. The presence of urea is shown by an increase in the ammonia content after adding urease (see below). That all of the ammonia and urea in the stool is produced by bacterial proteolysis is certainly open to question. The intestinal ferments split ammonia from the "amid fraction" of the protein molecule. Whether the small amount thus produced is absorbed before reaching the stool mass in the large intestine is not known. There is also some evidence that ammonia is excreted to a slight extent into the upper part of the intestine and that in some conditions of disease, nephritis, for instance, the amount may be con-

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* From the wards of the Boston Floating Hospital and from the Children's Department of the Massachusetts General Hospital.

1. Kendall, Arthur I, and Walker, Arthur W.: Determination of Urea Nitrogen in Cultures of Certain Bacteria, *Jour. Biol. Chem.*, August, 1913, p. 277.

siderable. On the other hand, Folin and Denis² by experiments with cats have demonstrated that ammonia is absorbed from the large intestine when it contains feces. They have also found that solutions of urea are rapidly absorbed from an empty large intestine.³ Whether urea may under certain conditions be excreted into the intestine is not known. Although the balance between possible excretion and proved absorption of these substances is not known, it is probable that the amounts of ammonia and urea found in the stool represent fairly closely the extent, possibly not the full extent rather than the reverse, of bacterial proteolysis in the large intestine.

That total nitrogen determinations in the stool may contain an error due to loss of ammonia nitrogen from the specimen has been well recognized, and precautions are advised for the prevention of this during the collection, storage and drying of stools. Since the determination of nitrogen balance is often an essential point in metabolism experiments, and since the size of the error which may be caused by the loss of ammonia nitrogen is not at all definitely known, it has seemed to us worth while to determine the usual—and unusual—amounts of ammonia which may be found in fresh stools, the pace at which it increases while the stool is stored, and the amount which may be driven off during drying.

It was thought, moreover, that a simple method of determining the ammonia content of fresh stools might be useful in another direction. The necessary ability which bacteria have of metabolizing protein has been given the uncomfortable name "putrefaction." While the digestive ferments do not split protein further than the amino-acid stage, bacteria are able to carry the process to completion by decomposing these *Bausteine* of the protein molecule. From amino-acids of the aromatic type they produce substances—phenol, indol, skatol, and others—which if absorbed from the intestine are suspected of causing harm to the organism unless it protects itself by conjugating them with sulphuric or glycuronic acid and excreting them as inert esters—ethereal sulphates, chiefly—in the urine. (It should be mentioned here that although these derivatives of tyrosin, tryptophan, and phenylalanin are not produced by the digestive ferments, it is likely that they are formed within the body during the ultimate catabolism of these amino-acids.) As it would seem fair to take the ammonia content of fresh stools as an index of the extent of intestinal putrefaction, and as the method for determining ammonia in stools described below is rapid and simple, it is suggested that such determinations would be

2. Folin, Otto, and Denis, W.: The Origin and Significance of Ammonia in the Portal Blood, *Jour. Biol. Chem.*, March, 1912, p. 161.

3. Folin, Otto, and Denis, W.: Absorption from the Large Intestine, *Jour. Biol. Chem.*, August, 1912, p. 253.

useful in the study of cases clinically labeled "intestinal auto-intoxication," "intestinal toxemia," etc.

The literature contains scant information as to the amount of ammonia found in fresh stools. Brauneck,⁴ in 1886, reported the average amount of ammonia in stools from normal adults to be 0.151 per cent. of the dried stool, and that stools from nephritics contained on the average 0.343 per cent. He used the old Schlösing method for determination of ammonia in the urine. The stool sample was made acid with hydrochloric acid and dried. A hot water digest was made from the powdered stool, and lead acetate added. The filtrate, after setting free the ammonia in it by adding milk of lime, was placed in a flat dish under a bell-jar and over another dish containing fourth-normal sulphuric acid. After five days the ammonia taken up by the sulphuric acid was measured by titration. H. Bartling,⁵ using undried samples in which he set the ammonia free by adding soda and collected it in tenth-normal hydrochloric acid by distilling under vacuum at 42 C., found in stools from an adult, on ordinary diet, who was normal except for anemia, an ammonia content of 0.398 per cent. of dried substance. After the addition to the diet of 300 gm. calf's thymus the ammonia rose to 0.625 per cent. The total nitrogen in the stool, however, was not increased, so that the ammonia nitrogen in per cent. of total nitrogen rose from 4.9 per cent. when on ordinary diet to 8.3 per cent. when extra protein was given. Both these workers regarded the ammonia found in feces as excreted from the wall of the intestinal tract.

METHODS OF PROCEDURE

Method of Collecting Specimens.—The baby was placed on a Bradford frame in the manner which has been described by Talbot.⁶ The stools were collected for a period of twenty-four hours, beginning at 9 o'clock in the morning. The receiving cup was inspected at hourly intervals by a nurse, and when found to contain feces was removed and placed directly on ice, another cup taking its place in order to keep the stools as fresh as possible. The urine was collected separately. The determinations for total nitrogen, ammonia, and urea nitrogen were carried out within a few hours after completion of the twenty-four hour collection period.

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6. Talbot, Fritz B.: Apparatus for Metabolism Experiments in Male Infants, Jour. Am. Med. Assn., Nov. 27, 1909, p. 1818.

Method of Analysis.—Total nitrogen: The following modification of Folin's micro-Kjeldahl method for total nitrogen in the urine was devised and found to give very satisfactory results. The twenty-four hour specimen of stool is placed in a weighed dish and thoroughly mixed by stirring and rubbing with a spatula, water being added if necessary. Its weight is then determined and a 2 to 5 gm. sample weighed out in a small evaporating dish, over this is poured from 60 to 70 c.c. 20 per cent. sulphuric acid and the dish placed on the water-bath for from one-half to one hour. The resulting digest is then transferred to a 100 c.c. volumetric flask, cooled and made up to the mark with 20 per cent. sulphuric acid. From this two 5 c.c. samples are pipetted into large Jena glass test tubes, and 1 gm. potassium sulphate, two drops 10 per cent. copper sulphate and a small pebble added to each. No sulphuric acid need be added as enough is contained in the samples. The tubes are then placed over micro-burners and from this point the determination is carried on as in the method for urine. The digestion mixture should be boiled carefully at first in order to avoid driving it very far up the sides of the tubes. Digestion will be found to be complete in twenty or twenty-five minutes. One point which is not quite satisfactory must be mentioned. The preliminary digest often contains minute particles which tend to settle, and for this reason the mixture must be shaken immediately before pipetting the samples. All danger of error may be avoided by carrying out the preliminary digestion in a small Kjeldahl flask over a flame, and this plan must be followed when the stool contains casein curds. It was found, however, that duplicates from the usual type of stool, digested on the water-bath, were in close agreement, and also agreed with the result obtained by carrying through a sample by the regular Kjeldahl method. While no essential advantages can be urged, it will be found that as compared with the usual way of doing Kjeldahls, this modification is shorter and less cumbersome, and where other colorimetric nitrogen determinations are being carried out at the same time, it fits conveniently into laboratory routine. The micro-method can also be very conveniently used for determination of total nitrogen in milk, in which case no preliminary digestion is necessary. The milk is simply diluted until 5 c.c. will contain about 1 mg. of nitrogen.

Ammonia Nitrogen: At the suggestion of Dr. Denis, the Folin method for ammonia in the urine was used. Folin and Denis have employed it occasionally for the determination of ammonia in feces in the course of animal experiments. The steps are very simple. A 1 or 2 gm. sample of well mixed stool is weighed out on a small bit of oiled paper. The paper and sample are then dropped into a large test-tube, and about 5 c.c. of water added. If the stool is fluid, it is

weighed in a small porcelain dish and rinsed into the test tube with 5 c.c. of water. A few drops of kerosene and 1 or 2 c.c. of a solution containing 15 per cent. potassium oxalate and 15 per cent. potassium carbonate are then added and the determination carried on as in the method for urine, except that the air current is allowed to run twenty minutes instead of ten. All determinations were made in duplicate and the results averaged. In most of the stools examined the agreement between duplicates was within 3 per cent. Considering that the samples were small and weighed separately on an ordinary inexpensive balance, such a result is satisfactory, and is interesting as showing the very uniform composition of the usual type of infants' stool. Stool containing casein shreds and curds gave a difference between duplicates of from 5 to 10 per cent.

Urea Nitrogen: A 1 or 2 gm. stool sample was placed in a large test-tube with 5 c.c. of water, 1 c.c. of 15 per cent. "Arlco-urease" and a few drops of kerosene. It was then stoppered and connected with the compressed air tap and allowed to stand thirty minutes at room temperature with a rather slow air current passing through it, for the purpose of breaking up the stool sample. A receiving tube, containing 2 or 3 c.c. of tenth-normal hydrochloric acid, was of course in position. One or 2 c.c. of the potassium oxalate and carbonate solution were then added through the inlet tube and the blowing resumed vigorously for twenty minutes. From the ammonia nitrogen obtained was subtracted that found in a sample similarly prepared, but without the addition of urease. The difference was regarded as urea nitrogen. That this is the case cannot be accepted without reservation. Marshall⁷ has shown the specific action of urease on urea in the urine. That this holds true among the many nitrogen-containing compounds present in feces is probably the case, but would be an extremely difficult point to prove. Duplicate determinations for urea were found to agree with the same closeness as in the case of ammonia.

RESULTS AND DISCUSSION

The Usual Ammonia Content of Infants' Stools and Its Relation to the Amount of Protein in the Diet.—In Table 1 are given thirty-seven determinations of total nitrogen and ammonia nitrogen from twenty-four hour stool specimens. It being realized that the day-to-day amount of stool passed must vary considerably, the amounts of nitrogen and ammonia per gram of dried stool are also given. These later figures probably afford a better basis for comparison but are not entirely satisfactory because of being affected by the variable amount

7. Marshall, E. K., Jr.: A Rapid Clinical Method for the Estimation of Urea in the Urine, Jour. Biol. Chem., April, 1913, p. 283.

TABLE 1.—THIRTY-SEVEN DETERMINATIONS OF TOTAL NITROGEN AND AMMONIA NITROGEN FROM TWENTY-FOUR-HOUR STOOL SPECIMENS

| Number | Gm. Protein per Kilo in Food | Nitrogen in Stools | | Ammonia N. in Stools | | Ammonia N.: Total N. Per Cent. |
|--------|--|---------------------------------|----------------------------------|---------------------------------|----------------------------------|---|
| | | Total for 24 Hours mg. | Per Gm. Dried Stool mg. | Total for 24 Hours mg. | Per Gm. Dried Stool mg. | |
| 13.3 | 1.2 | 102 | 53 | 5 | 2.4 | 5.0 |
| 11.4 | 1.7 | 218 | 53 | 16 | 3.9 | 7.9 |
| 23.2 | 1.8 | 191 | 24 | 21 | 2.6 | 11.0 |
| 19.1 | 2.0 | 488 | 44 | 23 | 2.1 | 4.7 |
| 5.1 | 2.3 | 298 | 25 | 29 | 2.5 | 9.7 |
| 9.2 | 2.4 | 750 | 54 | 47 | 3.4 | 6.3 |
| 13.1 | 2.9 | 360 | 63 | 19 | 3.3 | 5.3 |
| 10.2 | 2.0 | 203 | 24 | 23 | 2.7 | 11.3 |
| 1.3 | 2.9 | 417 | 39 | 39 | 3.6 | 9.4 |
| 24.1 | 3.6 | 216 | 42 | 16 | 3.1 | 7.4 |
| 10.1 | 3.8 | 480 | 38 | 61 | 4.8 | 12.7 |
| 6.1 | 4.1 | 230 | 40 | 25 | 4.4 | 11.9 |
| 25.1 | 4.2 | 312 | 58 | 31 | 5.7 | 10.0 |
| 1.1 | 4.5 | 347 | 26 | 16 | 1.2 | 4.6 |
| 18.1 | 4.6 | 501 | 35 | 43 | 3.0 | 8.6 |
| 5.2 | 4.4 | 427 | 39 | 53 | 4.8 | 12.4 |
| 5.3 | 4.8 | 492 | 38 | 40 | 3.1 | 8.1 |
| 17.1 | 5.0 | 215 | 67 | 17 | 5.3 | 1.9 |
| 24.2 | 5.0 | 384 | 42 | 40 | 4.3 | 10.4 |
| 24.3 | 5.0 | 653 | 53 | 53 | 4.3 | 8.1 |
| 11.1 | 5.2 | 625 | 41 | 49 | 3.2 | 7.9 |
| 8.1 | 5.2 | 417 | 37 | 46 | 4.1 | 11.0 |
| 4.1 | 5.3 | 118 | 29 | 3 | 0.7 | 2.5 |
| 3.1 | 5.3 | 447 | 27 | 67 | 4.0 | 15.0 |
| 13.2 | 5.4 | 305 | 46 | 35 | 5.2 | 11.5 |
| 19.2 | 5.5 | 259 | 67 | 33 | 9.9 | 12.7 |
| 5.4 | 5.9 | 640 | 46 | 61 | 4.4 | 9.5 |
| 16.1 | 6.1 | 202 | 37 | 17 | 3.1 | 8.4 |
| 11.3 | 6.5 | 648 | 43 | 54 | 3.6 | 8.3 |
| 11.2 | 6.6 | 710 | 50 | 72 | 5.0 | 10.1 |
| 5.5 | 7.1 | 1,159 | 65 | 85 | 4.7 | 7.3 |
| 20.2 | 8.0 | 451 | 68 | 55 | 8.3 | 12.2 |
| 10.4 | 8.6 | 298 | 93 | 37 | 11.6 | 12.4 |
| 10.3 | 8.6 | 170 | 35 | 11 | 2.2 | 6.5 |
| 23.3 | 8.9 | 571 | 65 | 33 | 3.8 | 5.8 |
| 23.1 | 9.5 | 1,436 | 126 | 65 | 5.7 | 4.5 |
| 23.2 | 9.5 | 628 | 72 | 63 | 7.2 | 10.0 |

of fat in the stool. The data are arranged with reference to an increasing protein intake. The babies supplying these specimens were all practically normal, that is, they came to the hospital without history of serious nutritional disturbance and when their food was regulated they gained weight in the normal way. Four of them, Nos. 20.2, 23.1, 23.2, and 24.3, were given buttermilk, and three, Nos. 16.1, 17.1, 19.2, received Eiweiss milk. The rest were on ordinary modifications of cow's milk. In a good many instances several specimens were obtained from the same baby, as is indicated in the number column by recurrence of the same figures in the integral part of the numbers. The age of the babies was between 2 and 10 months. A glance at the table will show that the ammonia content is widely variable but tends to grow larger as the protein intake is increased.

TABLE 2.—AVERAGES OF GROUPS INDICATED IN TABLE 1

| No. Observations | Protein Gm. per Kilo in Food | Gm. Carbo-hydrate per Kilo in Food | Nitrogen in Stools | | Ammonia N. in Stools | | Ammonia N.: Total N. Per Cent. |
|------------------|------------------------------|------------------------------------|--------------------|-------------------------|----------------------|-------------------------|--------------------------------|
| | | | Total mg. | Per Gm. Dried Stool mg. | Total mg. | Per Gm. Dried Stool mg. | |
| 6 | 1.9 | 13 | 341 | 42 | 23 | 2.8 | 7.4 |
| 11 | 3.9 | 13 | 362 | 40 | 33 | 3.6 | 9.3 |
| 13 | 5.5 | 11 | 432 | 45 | 42 | 4.4 | 9.5 |
| 7 | 8.6 | 11 | 673 | 76 | 50 | 6.2 | 8.4 |
| 37 | 5.0 | 12 | 443 | 52 | 38 | 4.2 | 9.0 |

This is very evident in Table 2, in which the groups indicated in Table 1 are averaged. In the first three groups the total nitrogen per gram dried stool is about the same. Apparently as much as 5.5 gm. protein per kilo is nearly as completely utilized as 1.9 gm. It must also be admitted that the increase in ammonia content as more protein is utilized could be interpreted as evidence that the excretion factor may be larger than we are assuming. Except when buttermilk or Eiweiss milk was given, the babies received a usual amount of carbohydrate. The average amount in grams per kilo is given in this table, and will be seen to be nearly the same for the four groups. According to the views of Kendall⁸ based on culture-flask experiments, if a sufficient amount of carbohydrate is available bacteria will utilize it for their vegetative needs and metabolize protein only to the extent necessary for the maintenance of their chemical structure, no matter how

8. Kendall, Arthur L., and Farmer, Chester J.: Studies in Bacterial Metabolism, viii, Jour. Biol. Chem., October, 1912.

much of it may be at hand. Interpreting the results presented here in this light, we must assume that when the usual amount of carbohydrate is fed babies, the portion of it escaping absorption and reaching the large intestine is altogether inadequate to supply fuel for the vegetative functions of the bacteria. Kendall's experiments are quite convincing on the point that bacteria prefer to metabolize carbohydrate up to a certain point, rather than the nitrogenous substances contained in bouillon, but whether enough carbohydrate can be given a baby, without overtaking its tolerance for it, to bring about in the lower bowel an imitation of his culture-flask conditions, seems to us problematical. Average figures for the thirty-seven specimens are also presented. It will be seen that the average ammonia nitrogen content was 38 mg. or 4.2 mg. per gram of dried stool. The highest ten in the series gave an average of 64 mg. or 6.8 mg. per gram dried stool, and

TABLE 3.—AVERAGE AMMONIA CONTENT FOR THREE GROUPS ARRANGED ACCORDING TO THE NUMBER OF STOOLS PASSED

| No. Observations | Gm. Protein in Food per Kilo | Number of Stools 24 Hours | Nitrogen in Stools | | Ammonia N. in Stools | | Ammonia N.: Total N. Per Cent. |
|------------------|------------------------------|---------------------------|--------------------|-------------------------|----------------------|-------------------------|--------------------------------|
| | | | Total mg. | Per Gm. Dried Stool mg. | Total mg. | Per Gm. Dried Stool mg. | |
| 9 | 5.3 | 1 | 321 | 46 | 27 | 3.3 | 7.6 |
| 12 | 5.4 | 2-4 | 322 | 55 | 34 | 5.5 | 10.0 |
| 15 | 4.9 | 5-10 | 608 | 48 | 48 | 3.7 | 8.6 |

the lowest ten 14 mg. or 2.3 mg. per gram dried stool. The average for ammonia nitrogen in per cent. of total nitrogen was 9.0, and in per cent. of dried stool substance 0.42.

Ammonia Content in Relation to Number of Stools Passed.—The results were rearranged in three groups according to the number of stools in twenty-four hours. The averages for these groups are given in Table 3. The amount of protein in the food was, in average, about the same in the three groups. It will be seen that the ammonia content increases as the stools become more frequent. That the ammonia per gram dried stool is not higher in the third group than in the second is undoubtedly due to the large amount of unutilized fat in the stools when they are very frequent. The increase in the extent of putrefaction is probably due to the fact that more nitrogenous material escapes absorption, and to the better opportunity for bacterial activity afforded by the more fluid texture of the stools. That constipated stools contain the least ammonia is interesting, because of the prevailing suspicion that constipation is an ally of intestinal putrefaction.

TABLE 4.—FOUR CASES OF STOOLS WITH UNUSUALLY HIGH AMMONIA CONTENT

| Diagnosis | Food | Gm. Protein per Kilo in Food | Number Stools 24 Hours | Nitrogen in Stools | | Ammonia N. in Stools | | Ammonia Total N. Per Cent. |
|-------------------|------------------|---------------------------------------|------------------------------|--------------------|----------------------------------|----------------------|----------------------------------|----------------------------------|
| | | | | Total mg. | Per Gm. Dried Stool mg. | Total mg. | Per Gm. Dried Stool mg. | |
| Indigestion | Buttermilk | 8.0 | 6 | 1,556 | 98 | 237 | 15.0 | 15.2 |
| Malnutrition .. | Eiweiss | 8.2 | 3 | 620 | 55 | 150 | 13.3 | 24.0 |
| Atrophy | Buttermilk | 5.4 | 6 | 770 | 87 | 168 | 19.0 | 22.0 |
| Atrophy | 1.5-6-1.2 | 5.8 | 11 | 1,022 | 42 | 148 | 6.0 | 14.5 |

Stools with Unusually High Ammonia Content.—Four such were encountered—see Table 4. Three were from babies in an advanced stage of malnutrition, the large amount of unutilized protein reaching the lower part of the intestine, as shown by the high nitrogen content of the stools, is probably a sufficient explanation of the unusual degree of putrefaction. It is worth noting, to the discredit of its alleged efficacy in reducing intestinal putrefaction, that two of these babies were receiving buttermilk.

Increase in Ammonia in Stools on Standing.—The extent of this is shown in Table 5. It will be seen there that the amount of ammonia

TABLE 5.—INCREASE IN AMMONIA IN STOOLS ON STANDING

| NH ₃ Nitrogen Fresh Stools | | NH ₃ Nitrogen 24 Hours After Collection | | NH ₃ Nitrogen 48 Hours After Collection | |
|---------------------------------------|--------------------------|--|--------------------------|--|--------------------------|
| Total mg. | Per Cent. Total Nitrogen | Total mg. | Per Cent. Total Nitrogen | Total mg. | Per Cent. Total Nitrogen |
| STOOLS STANDING AT ROOM TEMPERATURE | | | | | |
| 26 | 5 | ... | ... | 41 | 8 |
| 55 | 12 | 87 | 19 | 110 | 24 |
| 71 | 5 | 167 | 12 | 212 | 15 |
| 40 | 10 | 67 | 17 | ... | ... |
| 21 | 11 | ... | ... | 42 | 22 |
| 31 | 10 | ... | ... | 74 | 24 |
| STOOLS STANDING IN ICE-BOX | | | | | |
| 26 | 5 | ... | ... | 31 | 6 |
| 16 | 7 | ... | ... | 17 | 8 |
| 54 | 8 | ... | ... | 80 | 12 |
| 33 | 6 | ... | ... | 35 | 6 |

found in stools standing at room temperature for forty-eight hours was two or three times as much as the stools when fresh. Stools stored for the same length of time in the ice-chest showed only a very slight increase in the amount of ammonia contained.

Loss of Ammonia from Stools while Standing.—Twenty gram samples from six stools were placed in 200 c.c. Erlenmeyer flasks. Each flask was closed by a rubber stopper through which passed two pieces of glass tubing. The outer ends of the tubing were closed by slipping rubber tubing over them and clamping it. The samples were left standing at room temperature for forty-eight hours. The flasks were then connected with the compressed-air tap, and the air inside them driven out, and into a test tube containing a few cubic centimeters

of tenth-normal hydrochloric acid. Three of the stools were alkaline and three acid. On testing, in each case, the hydrochloric acid in the receiving tube with Nessler's reagent it was found that from two of the alkaline stools a trace of ammonia—not measurable in the colorimeter—had been collected. No ammonia had been given off from the other four specimens. Evidently then there is not much danger of loss of ammonia from stools stored in closed vessels.

Loss of Ammonia from Stools during Drying.—A ten gm. sample of fresh stool was spread over the bottom of a 200 c.c. Erlenmeyer flask, provided with a rubber stopper carrying inlet and outlet tubes as described as above. The flask was then placed on the water-bath

TABLE 6.—LOSS OF AMMONIA FROM STOOLS DURING DRYING

| Reaction | Total Nitrogen in Fresh Stool mg. | Ammonia Nitrogen in Fresh Stool mg. | Ammonia Nitrogen Collected During Drying | | Nitrogen in Dried Stool + Ammonia Nitrogen Collected mg. | Ammonia Nitrogen in Dried Stool mg. |
|----------|-----------------------------------|-------------------------------------|--|--------------------------|--|-------------------------------------|
| | | | Total mg. | Per Cent. Total Nitrogen | | |
| Alk. | 202 | 17 | 17 | 8.4 | 211 | |
| Alk. | 1,556 | 237 | 341 | 21.9 | 1,562 | |
| Ac. | 417 | 39 | 34 | 8.2 | 401 | |
| Ac. | 710 | 72 | 89 | 12.5 | 713 | |
| Ac. | 501 | 43 | 9 | 1.8 | 498 | |
| Alk. | 800 | 71 | 62 | 7.8 | 780 | 6 |
| Alk. | 648 | 54 | 83 | 12.8 | 642 | 9 |
| Ac. | 488 | 23 | 6 | 1.2 | 486 | 18 |
| Alk. | 215 | 17 | 36 | 16.8 | 193 | |
| Ac. | 295 | 50 | 43 | 14.6 | ... | 8 |
| Ac. | 620 | 150 | 89 | 14.4 | | |
| Alk. | 451 | 55 | 67 | 14.9 | | |
| Alk. | 628 | 63 | 72 | 11.5 | | |
| Alk. | 1,436 | 65 | 42 | 2.9 | | |
| Alk. | 653 | 53 | 66 | 10.1 | | |
| Alk. | 203 | 23 | 28 | 13.8 | | 5 |

and connected with the compressed-air tap. A slow current of air was allowed to pass through the flask, and then through the tenth-normal hydrochloric acid in a receiving tube, while the stool sample was drying. The ammonia collected in the receiving tube was then measured by adding Nessler's, making up to an appropriate volume and reading in the colorimeter. The results of a series of these experiments are given in Table 6. The figures for total nitrogen and ammonia nitrogen are for the twenty-four hour specimen. It was found that the acid stools lost a large part of their ammonia, and that from the alkaline stools more ammonia was usually collected than the stools contained before drying. That the cause of this ammonia

production during drying is bacterial activity does not seem likely as the time required was short—from one and a half to two hours—and the decreasing moisture in the stool unfavorable to bacterial activity. It would seem more probable that the extra ammonia is derived from some nitrogenous substance or substances decomposed by the heat and drying. It is possible that its chief source may be urea. The urea contained in two of the specimens in the series was measured and found to be 20 and 16 mg. The extra ammonia collected from these two was 12 and 13 mg. A few determinations, given in the last column in the table, showed that some ammonia was still contained in the dried stool. A comparison of the figures in column 6 in

TABLE 7.—UREA NITROGEN IN FIFTEEN TWENTY-FOUR-HOUR STOOLS

| Total Nitrogen mg. | Ammonia Nitrogen mg. | Urea Nitrogen Total mg. | Urea Nitrogen per gm. Dried Stool mg. | Urea N.; Total N. Per Cent. |
|--------------------|----------------------|-------------------------|---------------------------------------|-----------------------------|
| 170 | 11 | 8 | 1.0 | 4.7 |
| 298 | 37 | 11 | 3.4 | 3.7 |
| 295 | 50 | 13 | 1.9 | 4.4 |
| 268 | 7 | 15 | 4.4 | 5.6 |
| 488 | 23 | 10 | 0.9 | 2.0 |
| 259 | 33 | 4 | 1.0 | 0.6 |
| 620 | 150 | 24 | 2.1 | 3.9 |
| 451 | 55 | 20 | 3.0 | 4.4 |
| 1,436 | 65 | 12 | 1.1 | 0.8 |
| 191 | 21 | 9 | 1.1 | 4.7 |
| 571 | 33 | 15 | 1.7 | 2.6 |
| 216 | 16 | 9 | 1.8 | 4.2 |
| 384 | 40 | 12 | 1.3 | 3.1 |
| 653 | 53 | 16 | 1.3 | 2.5 |
| 312 | 31 | 16 | 3.0 | 5.1 |

this table with those in column 2 will show fairly well the degree of accuracy, attained by the micro-Kjeldahl method for total nitrogen.

From these experiments we conclude that there is practically no danger of loss of ammonia nitrogen from stools during collection and storage, unless the specimen is allowed to lose moisture; but that during drying a very serious loss may occur, often as much as from 15 to 20 per cent. of total nitrogen from fresh stools, while from stools left standing for two days at room temperature one half of the total nitrogen may escape measurement. For the prevention of this loss the addition of preservatives is obviously inefficient. The only measure which has a sound basis is the addition of non-volatile acid with the object of fixing the ammonia. This was tested and found to be nearly always completely efficient provided enough acid was thoroughly mixed in the stool. It should be remembered that the texture of the stool

substance offers obstacles to diffusion and that as its particles dry, ammonia escaping from them may in the absence of water escape contact with the acid. Adding a crystal or two of oxalic acid or a few drops of weak hydrochloric acid is not by any means sufficient, even though this may make the stool acid to litmus. Five c.c. of 2 per cent. hydrochloric acid well mixed with 10 gm. of stool was found to prevent any loss of ammonia from stools of the usual type but not from those containing casein shreds and curds. Since the danger of losing nitrogen is entirely avoided by making the determinations from an undried sample we prefer the wet method. We are convinced that as even a sample is obtained from the fresh as from the dried and powdered stool in most instances. There is certainly less chance for error in weighing a 5 to 10 gm. sample of fresh stool than comes into the process of grinding up the dried stool, determining its weight and

TABLE 8.—INCREASE IN UREA IN STOOLS STANDING SEVERAL DAYS AT ROOM TEMPERATURE

| Urea N in Fresh Stool mg. | Urea N 24 Hours After Collection mg. | Urea N 48 Hours After Collection mg. | Urea N Three Days After Collection mg. | Urea N Five Days After Collection mg. |
|------------------------------------|--|--|--|---|
| 10 | .. | .. | 7 | 33 |
| 20 | 5 | 12 | .. | .. |
| 14 | 5 | .. | 93 | 122 |
| 9 | .. | 14 | .. | 28 |
| 12 | .. | 21 | .. | .. |
| 16 | .. | 26 | .. | .. |

then weighing out a 0.25 to 0.50 gm. sample of the dusty hygroscopic powder. Moreover, by the former procedure one escapes the very frequent annoyance of encountering stools which, because of the neutral fat they contain, will not powder, unless they are dried with sea-sand or plaster of Paris, thus introducing another source of error. Even in the case of stools containing much mucus or casein curds we prefer to make a preliminary digest of a large sample and determine the nitrogen in a measured portion of this rather than trust to the evenness of a sample of stool powder.

The Urea Content of Stools.—Urea nitrogen was determined in fifteen twenty-four hour specimens from practically normal babies. The amounts found are given in Table 7. The average for the fifteen stools was 13 mg. or 2.0 mg. per gram dried stool. The average in per cent. of total nitrogen was 3.5. As may be seen in the table, the proportionate relationship between urea nitrogen and ammonia nitro-

gen is widely variable. Whether or not some of the urea found in stools was excreted by the intestinal wall, we are unprepared to say. That the intestinal flora are capable of producing urea is evident from an increase in the amount of it found in stools standing several days at room temperature. Determinations showing this are given in Table 8.

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FORMS OF NITROGEN IN THE STOOLS OF INFANTS *

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It has for some time been recognized that the *amount* of nitrogen lost in the stools of infants is rarely of great importance from the point of view of nutrition. The percentage of the intake which escapes absorption seldom constitutes a serious loss. It seemed possible, however, that significant information concerning the manner in which the alimentary tract handles the food proteins under varying conditions might be obtained by a study of the relative *proportions* of the fecal nitrogen which are excreted in the form of protein, and of amino acids and ammonia, the two chief final split products of protein. When proteins are digested under aseptic conditions by the intestinal enzymes, trypsin and erepsin, amino acids are the main products, and the amount of ammonia is relatively small. Putrefactive bacteria, on the other hand, are capable of changing a large percentage of the nitrogen of proteins and amino acids into ammonia. Consequently an increase of ammonia in the fecal nitrogen at the expense of the amino acids might serve as an indication of the activity of putrefactive bacteria. A relatively high proportion of amino acids, on the other hand, might indicate incomplete absorption of the protein digestion products, despite complete digestion and absence of putrefaction.

Our results failed to show any constant relations between the clinical condition of the patients and the distribution of the fecal nitrogen among the three forms discussed above. The data obtained are, however, not without interest in their revelation of the form in which the unabsorbed nitrogen leaves the alimentary canal, particularly as previous information on this point has been very meager.

METHODS

The method of collection made it almost impossible for a urine contamination to occur without our knowledge. The stools were used either when freshly voided or were placed at once in an ice-box to

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* From the Laboratories of the Rockefeller Institute and the Babies' Hospital.

* The observations reported here were begun in the fall of 1913, and have since been continued at intervals as cases suitable for study have presented themselves.

avoid any further decomposition. Forty to 50 gm. of the fresh feces were emulsified in water and diluted to 200 c.c. The mixture was made homogeneous by grinding in a mortar and aliquot portions were taken for the following determinations.

Total Nitrogen.—Five c.c. were used for a Kjeldahl determination.

Ammonia.—Ten c.c. were placed in a 100 c.c. test tube, 4 to 5 gm. of potassium carbonate, with 2 drops of octyl alcohol to prevent foam, were added, and the ammonia was determined by aeration into fiftieth-normal acid by Folin's method.

Urea.—Ten c.c. were placed in a 100 c.c. test tube with 5 c.c. of 0.6 per cent. KH_2PO_4 and 1 c.c. of 10 per cent. "Arco-urease."¹ After fifteen minutes, allowed for hydrolysis of the urea, from 8 to 10 gm. of potassium carbonate were added and the ammonia aerated into fiftieth-normal acid. The increase in ammonia resulting from the action of the urease represents the urea nitrogen. The accuracy of the method under the conditions described was shown by control analyses on ten specimens of feces. Known amounts of urea were added to measured portions of the emulsified feces. In every case the determinations showed an increase in urea equal to the amount added.

Free Amino Acid Nitrogen.—To 100 c.c. of emulsion about 0.5 gm. of charcoal was added, and the solution was filtered without washing the residue. The volume of the filtrate was measured, and to it 10 per cent. metaphosphoric acid was added until all the protein was precipitated. The volume of metaphosphoric acid solution required was 15 c.c. or less. After a half hour had been allowed for complete precipitation of the proteins, the mixture was made up to a convenient volume, made alkaline by addition of powdered calcium hydroxid, and filtered. The filtrate was free from protein, as indicated by the biuret test. The filtrate was measured and evaporated to dryness on a water bath. During evaporation the solution, made alkaline by the above mentioned addition of lime, entirely loses its ammonia. The foregoing treatment therefore frees the solution of both protein and ammonia. The dry residue was taken up with 1 c.c. of 50 per cent. acetic acid and washed into a 10 c.c. measuring flask with small portions of water. Two c.c. portions were used for determination of amino nitrogen by the nitrous acid method.²

Total Amino Acid Nitrogen after Hydrolysis of the Proteins.—Ten c.c. of the feces suspension were mixed with 10 c.c. of concentrated hydrochloric acid, and the solution, in a loosely stoppered tube, was immersed in a water bath at 100° for twenty-four hours. This

1. Van Slyke and Cullen: A Permanent Preparation of Urease and Its Use in the Determination of Urea, *Jour. Biol. Chem.*, 1914, xix, 211.

2. Van Slyke: *Jour. Biol. Chem.*, 1913, xvi, 121.

assures practically complete hydrolysis of the proteins present.³ The solution was evaporated to dryness on the water bath to remove the hydrochloric acid. The residue was taken up with water, made alkaline with calcium hydroxid, and filtered. The alkaline filtrate was concentrated to dryness to remove the ammonia. It was then redissolved with the help of 1 c.c. of 50 per cent. acetic acid; the solution was made up to 25 c.c., and 2 c.c. portions were taken for determination of amino nitrogen.

Acidity.—An aliquot part, usually 25 c.c., of the suspension of feces was titrated with tenth-normal sodium hydroxid, phenolphthalein being used as indicator. The method is, of course, a crude one, but yields comparable results.

DISCUSSION OF RESULTS

As the accompanying tables show, the proportion of the total nitrogen in the form of NH_2 of the *free amino acids* varies greatly, the range being from 1.8 per cent. to about ten times as much—17.6 per cent. The present data show no factor in the diet or condition of the patients which has an entirely constant effect on the proportion of nitrogen passing unabsorbed through the intestine either as ammonia or free amino acids. The more nearly normal babies showed low amino acid nitrogen, however, and those suffering from diarrhea generally showed the higher figures. None of the three breast-fed infants was among those eliminating a large proportion of amino acid nitrogen, and the only baby in the series that was both normal and breast-fed showed next to the lowest proportion of amino acid nitrogen in the feces. In the case that was followed for seven successive days (Table 2) it was noted that when the stools became loose the proportion of amino acids was increased, and vice versa. As a rule, to which there are exceptions, it appears that in the other cases also the more watery the stools the larger is the proportion of their nitrogen in the form of amino acids. Apparently the quicker passage through the alimentary tract results in a less complete absorption of the final products of protein digestion, viz., the amino acids.

In contrast to the wide variations above mentioned in the nitrogen of the free amino acids, the nitrogen of the *amino acids present after hydrolysis of the protein* was quite constant at from 43 to 55 per cent. of the total nitrogen. In a few exceptions this percentage was necessarily lower because the ammonia was so high. Most animal proteins when hydrolyzed show on the average about 75 per cent. of their nitrogen as free NH_2 , the other 25 per cent. being amid nitrogen and

3. Van Slyke: Conditions for the Complete Hydrolysis of Proteins, Jour. Biol. Chem., 1912. xii, 295.

TABLE 1.—FORMS OF—

| No. | Age in mos. | Condition | Food † |
|-----|------------------|--|---|
| 1 | 5 $\frac{3}{4}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour..... |
| 2 | 4 | Normal | Breast milk |
| 3 | 18 $\frac{1}{2}$ | Drowsy and feverish, improving very slightly. | Soft diet; egg, bread, cereal, sauce, milk. |
| 4 | 5 $\frac{1}{2}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour, and malt soup extract. |
| 5 | 8 $\frac{3}{4}$ | Convalescent from diarrhea..... | Protein milk |
| 6 | 19 $\frac{1}{4}$ | Feverish, with slight cough..... | 3-3.4-2.8 and cereal..... |
| 7 | 11 | Nearly normal after acute indigestion. | Protein milk with barley flour..... |
| 8 | 7 | Convalescent from enterocolitis..... | 1-4-1.75-1.2 (from condensed milk, boiled with sodium bicarbonate) with cane sugar and barley flour. |
| 9 | 6 $\frac{1}{4}$ | Slowly convalescent from wasting, diarrhea and vomiting. | 1.6-2-1.4 with barley flour (from condensed milk cooked with sodium bicarbonate). |
| 10 | 5 $\frac{3}{4}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour and malt soup extract. |
| 11 | 14 $\frac{3}{4}$ | Slowly convalescent from diarrhea and wasting. | Protein milk |
| 12 | 7 | Convalescent from diarrhea..... | Protein milk with barley flour and malt soup extract. |
| 13 | 1 | Congenital malformation of heart.... | 1-4-1.5-1.2, from condensed milk and boiled with sodium bicarbonate. |
| 14 | 6 $\frac{3}{4}$ | Convalescent from diarrhea and vomiting. | Protein milk with barley flour. Breast milk N3. |
| 15 | 5 | Marasmus, gaining slightly..... | Breast milk..... |
| 16 | 3 | Marasmus, gaining slightly..... | Breast milk..... |
| 17 | 3 | Marasmus, gaining slightly..... | Breast milk..... |
| 18 | 5 $\frac{1}{2}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour and malt soup extract. |
| 19 | 5 $\frac{1}{2}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour and malt soup extract. |
| 20 | 7 | Improving from diarrhea..... | Protein milk with barley flour and malt soup extract. |
| 21 | 5 $\frac{1}{2}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour and malt soup extract. |
| 22 | 25 $\frac{1}{2}$ | Suspected tuberculosis. Gaining weight. | House diet: scraped meat, potato, bread, cereal, sauce, milk. |
| 23 | 1 $\frac{1}{2}$ | Gaining slightly from wasting and vomiting. | 1-4-1.75-1.2 with barley flour (from condensed milk and boiled with sodium bicarbonate). |
| 24 | 6 $\frac{3}{4}$ | Slowly convalescent from wasting, diarrhea and vomiting. | 1.6-2-1.4 changed to 1.8-2.5-1.6 with malt soup extract. |
| 25 | 5 $\frac{1}{2}$ | Convalescent from diarrhea and wasting. | 2-4-1.8 with barley flour and malt soup extract. |
| 26 | 4 $\frac{3}{4}$ | Improving from diarrhea..... | Protein milk with cane sugar..... |
| 27 | 19 $\frac{1}{4}$ | Convalescent from bronchopneumonia. | Milk, two parts: water, one part..... |
| 28 | 19 $\frac{1}{2}$ | Convalescent from bronchopneumonia. | Soft diet; milk, egg, bread, sauce, cereal. |
| 29 | 8 | Convalescent from diarrhea..... | 1-4-1.75-1.2 from condensed milk and boiled with sodium bicarbonate and barley flour. Breast milk N4. |
| 30 | 12 | Convalescent from pneumonia..... | 3-5-2.8 with beef juice, cereal, orange juice and sweet wine of iron. |
| 31 | 7 $\frac{1}{2}$ | Improving slightly from diarrhea and vomiting. | 1.8-2.25-1.6 from condensed milk and boiled with sodium bicarbonate and cane sugar and barley. |
| 32 | 12 | Convalescent from pneumonia..... | 3-5-2.8 with beef juice, cereal, orange juice and sweet wine of iron. |
| 33 | 12 | Convalescent from pneumonia..... | 3-5-2.8 with beef juice, cereal, orange juice and sweet wine of iron. |
| 34 | 5 | Marasmus improving..... | Same as No. 35..... |
| 35 | 5 $\frac{1}{4}$ | Convalescent from bronchopneumonia. | 1-5-2 |
| 36 | 16 $\frac{1}{4}$ | Physically normal, mentally deficient.. | 2-6-5-2.4 and cereal..... |

* The cases are arranged in order corresponding to the free NH_2 figures, the lowest being given first.

† The figures for the food formulas are given in the order, per cent. of fat, per cent. of milk sugar, per cent. of protein.

—NITROGEN IN INFANTS' STOOLS *

| Stools | Gm. Total N per Gm. Dried Wt. | Per Cent. of Total N. as | | | Acidity c.c. N/10 NaOH |
|--|-------------------------------------|--------------------------|-------------------------------------|-------------------------|------------------------------|
| | | Free NH ₂ | NH ₂ After Hydrolysis | Free NH ₃ | |
| Formed, hard and dry..... | .071 | 1.8 | 46.9 | 8.1 | 0 |
| Watery in part; part pasty, greenish, sour. Soft curds. | .046 | 2.7 | 49.7 | 5.2 | 15.16 |
| Constipated, formed and hard.... | .055 | 2.9 | 55.1 | 7.7 | 1.84 |
| Mostly formed, hard and soapy in part. | .054 | 3.3 | 49.7 | 3.6 | 2.57 |
| Formed. Traces of mucus..... | .058 | 3.4 | 52.4 | 10.0 | 3.60 |
| Constipated, formed and hard.... | .064 | 3.7 | 52.0 | 18.8 | 3.05 |
| Part formed, in part smooth and pasty. | (.05) | 4.0 | | 12.0 | |
| Mostly formed, part pasty and smooth. | (.05) | 4.0 | | 13.0 | 2.70 |
| Very watery. Mucus and soft curds. | .046 | 4.6 | 50.4 | 10.6 | 1.88 |
| Mostly formed, soft and granular. | .073 | 4.8 | 43.4 | 6.9 | 3.13 |
| Part formed, part pasty. Large curds. | .049 | 4.9 | 51.8 | 27.9 | 2.49 |
| Part watery, part pasty, fermentative, acid. Mucus and curds. | .066 | 5.2 | 34.9 | | 4.65 |
| Very watery. Mucus and large soft curds. | .11 | 5.8 | 25.3 | 9.7 | 11.28 |
| Watery, large soft curds..... | .059 | 5.8 | 31.6 | 37.3 | 11.75 |
| Part formed, part thin, pasty.... | .046 | 6.2 | 50.6 | 7.8 | 14.59 |
| Watery, greenish, sour. Fat curds. | .065 | 6.3 | 47.6 | 5.9 | 9.65 |
| Watery, greenish, sour. Fat curds and mucus. | .059 | 6.4 | 47.4 | 3.8 | 10.61 |
| Watery and soft pasty, sour. Large soft curds. | .051 | 6.6 | 47.7 | 7.6 | 7.95 |
| Part formed, granular. Fine white curds. | .058 | 6.8 | 52.5 | 4.3 | 3.97 |
| Part formed, part thin, pasty, acid, fermentative, mucus. | .050 | 6.8 | | | 9.82 |
| Soft, pasty, granular. Soft curds. | .051 | 7.2 | 50.0 | 5.2 | 7.92 |
| Thin pasty, oily-appearing..... | .035 | 7.6 | 47.8 | 7.0 | 12.60 |
| Watery, full of fine white curds. Mucus. | .052 | 7.7 | 36.9 | 23.1 | 5.15 |
| Part formed, part watery. Soft curds and mucus. | .071 | 8.0 | 41.8 | 29.2 | .66 |
| Part formed, granular. Fine white curds. | .053 | 8.4 | 49.0 | 4.7 | 3.74 |
| Porridge-like, greenish..... | .029 | 9.0 | 50.4 | 19.5 | 7.37 |
| Mostly formed. Mucus..... | (.05) | 9.0 | | 13.0 | 2.60 |
| Pasty, granular, mucus..... | .057 | 9.6 | 48.8 | 15.0 | 8.20 |
| Watery, greenish, soft curds and mucus. | .065 | 10.2 | 55.5 | 7.6 | 9.30 |
| Watery, acid, foul, with small and large hard curds. | .052 | 10.7 | 41.4 | 12.8 | 7.59 |
| Mostly watery, granular, with fine white curds. | .049 | 13.3 | 52.6 | 8.8 | 7.48 |
| Very watery, greenish, with large, hard curds, soft curds and mucus. | .054 | 13.6 | 50.5 | 12.6 | 10.15 |
| Same as in No. 33..... | .059 | 13.8 | 45.6 | 9.0 | 10.72 |
| Part formed, partly thin, pasty, fermentative, mucus. | .058 | 14.3 | 46.4 | 17.2 | 9.67 |
| Watery, greenish, small soft curds. | (.05) | 16.0 | | 8.0 | 2.80 |
| Constipated, part formed and rather hard, part thin and smooth. | .038 | 17.6 | 44.1 | 9.2 | 1.30 |

the nitrogen of the amino acids, prolin, oxyprolin, tryptophan, arginin, and histodin, which have all or part of their nitrogen in forms other than NH_2 groups.⁴ Accordingly, if we multiply by 1.33 the amount of amino nitrogen found after acid hydrolysis of a mixture containing either animal proteins or their digestion products, we obtain approximately the amount of nitrogen present as protein and proteolytic products. Applying this factor (1.33) to our results for amino nitrogen after hydrolysis, we find that the feces on the average contain from 60 to 70 per cent. of their nitrogen in these forms. The

TABLE 2.—CASES FOLLOWED—

| Case | Condition | Date | Food |
|-------------------|--|---------------|---|
| E. V., 5½ mos. | Convalescent from diarrhea; doing well. Weight fluctuating, but rising on whole. | November 6.. | 2-4-1.8 with barley and malt soup extract |
| | | November 7.. | 2-4-1.8 with barley and malt soup extract |
| | | November 8.. | 2-4-1.8 with barley and malt soup extract |
| | | November 9.. | 2-4-1.8 with barley and malt soup extract |
| | | November 10.. | 2-4-1.8 with barley..... |
| E. W., 12 mos. | Convalescent from pneumonia. Gaining weight. | November 11.. | 2-4-1.8 with barley..... |
| | | November 12.. | 2-4-1.8 with barley..... |
| | | December 19.. | 3-5-2.8 with beef juice and cereal..... |
| | | December 20.. | 3-5-2.8 with beef juice and cereal..... |
| | | December 21.. | 3-5-2.8 with beef juice and cereal..... |

TABLE 3.—BREAST—

| Case | Condition | Date | Food |
|-------------------|---------------------------------|-------------------|------------------|
| G. R., 4 mos..... | Normal | December 22..... | Breast fed |
| A. R., 5 mos..... | Marasmus, gaining slightly..... | January 29..... | Breast fed |
| J. I., 3 mos..... | Marasmus, gaining slightly..... | Jan. 30-Feb. 2... | Breast fed |
| | | February 2-5..... | Breast fed |

free amino acid nitrogen alone constitutes from 2.4 to 24 per cent. of the total, while proteins, and possibly higher intermediate products, make up the balance.

The *urea* determinations were not performed on the same stools as the other determinations, for the reason that when the latter were done the *urea* method had not been entirely perfected. We have, however, determined the proportion of *urea* nitrogen in a separate lot of stools and present the results in table 4. They show that the proportion of the total nitrogen in the form of *urea* varies between 9 and 5.6 per cent. Nineteen out of the 25 stools contained no *urea* at all. That its absence

4. Van Slyke: Jour. Biol. Chem., 1911, x, 15: 1912, xii, 295.

was due to bacterial transformation of urea into ammonia appears unlikely, because some of the stools which contained no urea also contained but little ammonia. It should be stated that unless the separation between stools and urine is most carefully supervised, a high urea figure must be questioned.

The ammonia varies between 4 and 37 per cent. of the total fecal nitrogen. It usually equals or exceeds the amino acid nitrogen. This fact gives a definite basis for the accepted opinion that the fecal ammonia is of bacterial origin. When animal proteins, such as casein,

—ON SUCCESSIVE DAYS

| Stools | Gm. Total N. Per Gm. Dried Wt. | Per Cent. of Total N. as | | | Acidity c.c. N/10 NaOH |
|---|--------------------------------------|--------------------------|-------------------------------------|-------------------------|------------------------------|
| | | Free NH ₂ | NH ₂ After Hydrolysis | Free NH ₃ | |
| Part formed, granular. Fine white, curds. | .053 | 8.4 | 49.0 | 4.7 | 3.74 |
| Part formed, granular. Fine white, curds. | .058 | 6.8 | 52.5 | 4.3 | 3.97 |
| Mostly formed | .054 | 3.3 | 49.7 | 3.6 | 2.57 |
| Softer | .051 | 7.2 | 50.0 | 5.2 | 7.92 |
| Softer, large soft curds..... | .051 | 6.6 | 47.7 | 7.6 | 7.95 |
| Mostly formed again, though soft. | .073 | 4.8 | 43.4 | 6.9 | 3.13 |
| Entirely formed; hard and soapy.. | .071 | 1.8 | 46.9 | 8.1 | 0 |
| Watery; curds, acid, mucus..... | .052 | 10.7 | 41.4 | 12.8 | 7.59 |
| Watery; curds, acid, mucus..... | .059 | 13.8 | 45.6 | 9.0 | 10.72 |
| Watery; curds, acid, mucus..... | .054 | 13.6 | 50.5 | 12.6 | 10.15 |

—FED INFANTS

| Stools | Gm. Total N. Per Gm. Dried Wt. | Per Cent. of Total N. as | | | Acidity c.c. N/10 NaOH |
|------------------------------------|--------------------------------------|--------------------------|-------------------------------------|-------------------------|------------------------------|
| | | Free NH ₂ | NH ₂ After Hydrolysis | Free NH ₃ | |
| Watery, soft curds, yellow-green.. | .046 | 2.7 | 49.7 | 5.2 | 15.16 |
| Partly formed..... | .046 | 6.2 | 50.6 | 7.8 | 14.59 |
| Watery, fat curds..... | .065 | 6.3 | 47.6 | 5.9 | 9.65 |
| Watery, fat curds..... | .059 | 6.4 | 47.4 | 3.8 | 10.61 |

are split by non-bacterial agents, such as acids, or aseptic digestion with trypsin, the ammonia nitrogen is less than one-seventh the free NH₂ nitrogen.

No relation is perceptible between the proportion of ammonia and the condition of the patients or the nature of the stools. The amount of free amino acid nitrogen also bears no evident relation to the ammonia or to the acidity of the stools. The figures for each vary independently.

Nor does the acidity of the stools bear any observable relation to the ammonia. From the theory that fermentive and putrefactive bacteria are antagonistic, one would expect low ammonia when the acidity is high, and vice versa. It will be seen, however, that while this rela-

TABLE 4.—UREA DETERMINATIONS

| Name | Food | Description of Stool | Total N Per Gm. Dried Wt. | Ammonia N, Per Gm. Dried Wt. | Ammonia N, Per Cent. of Total N. | Urea N, Per Gm. Dried Wt. | Urea N, Per Cent. of Total N. |
|------------------|---|--|---------------------------------|------------------------------------|--|---------------------------------|-------------------------------------|
| L. D., 6 mos. | 1-6-4-1-4 with barley. | Soft, pasty. | .0390 | .00054 | 1.1 | 0 | 0 |
| V. C., 8 mos. | 1-8-2-2-2 with barley. | Watery. | .0302 | .00062 | 2.0 | .00033 | 1.1 |
| F. B., 5 mos. | Protein milk with rice flour and cane sugar. | Formed. | .0375 | .00130 | 3.6 | 0 | 0 |
| | | Part formed, part watery. | .0396 | .00060 | 1.4 | 0 | 0 |
| F. S., 7 mos. | 1-4-1-8 with barley. | Mostly watery. | .0488 | .00055 | 1.1 | 0 | 0 |
| A. A., 7 mos. | 1-6-5-2 with rice flour. | Watery and pasty. | .0493 | .00100 | 2.2 | 0 | 0 |
| Adh. A., 7 mos. | Protein milk with barley. | Mostly formed. | .0371 | .00080 | 2.2 | 0 | 0 |
| A. K., 8 mos. | Protein milk with barley and beet juice. | Part formed, part pasty. | .0373 | .00070 | 1.8 | 0 | 0 |
| J. E., 9 mos. | 2-5-1-8 | Formed. | .0445 | .00170 | 3.8 | 0 | 0 |
| J. F., 9 mos. | 2-6-5-2-4 | Soft, pasty, green, mucus. | .0682 | .00429 | 6.3 | .0011 | 1.6 |
| M. K., 1 mos. | 1-8-6-2-4 with barley. | Pasty, greenish brown, foul; mucus. | .0608 | .00433 | 7.1 | 0 | 0 |
| N. M., 7 mos. | Protein milk with barley. | Soft, pasty and watery, pale yellow. | .0632 | .00458 | 7.3 | 0 | 0 |
| N. M. | Protein milk with barley. | Mostly soft pasty, part watery, may be urine. | .0573 | .00609 | 10.6 | .00322 | 5.6 |
| S. J., 9 mos. | 2-4 with barley, 2 feedings. | Formed, but soft; mucus and bean curds. | .0403 | .00307 | 7.6 | 0 | 0 |
| R. A'II., 5 mos. | Protein milk with barley and cane sugar, 5 feedings; breast milk, 2 feedings. | Formed, pale yellow, part hard, Watery, pale yellow, with curds and mucus. | .0367 .0453 | .00198 .00487 | 5.4 10.7 | 0 .00117 | 0 2.6 |
| P. K., 4 mos. | 2-8-5-2-6 | Formed but soft, pale; bean curds. | .0504 | .00383 | 7.6 | 0 | 0 |
| M. L., 17 mos. | Soft diet. | Part formed, part watery; mucus | .0737 | .00392 | 5.3 | 0 | 0 |
| W. C., 3 mos. | Protein milk with barley and cane sugar. | Pasty, smooth; mucus. | | | 9.7 | 0 | 0 |
| A. II., 2 mos. | 1-6-5-2-0 | Very watery with fat curds and mucus. | .1026 | .00724 | 7.1 | 0 | 0 |
| L. A., 4 mos. | Breast milk; one feeding of pro- tein milk; with olive oil. | Very watery; oil floating on sur- face, bright yellow. | .0183 | .00395 | 21.6 | .00103 | 5.6 |
| R. P., 5 mos. | 2-5-1-8 with barley; breast milk, two feedings. | Part pasty, part watery; many fat curds. | .0513 | .00236 | 4.6 | 0 | 0 |
| C. S., 3 mos. | 1-8-5-1-6, four feedings; breast milk, three feedings. | Pasty; portion formed and hard; mucus. | .0462 | .00179 | 3.9 | 0 | 0 |
| E. K., 6 mos. | 1-2-4-2-2 | Part formed, constipated; part pasty, dark brown, smooth. | .0386 | .00351 | 9.1 | .00074 | 1.9 |

tionship exists in some cases, in others both ammonia and acidity are low, and in still others both are fairly high. In a few cases, such as No. 25, where a high ammonia content is accompanied by a low acidity, calculation indicates that the lack of acidity is due to the neutralization of acid by the unusual amount of ammonia, rather than to lack of acid formation.

SUMMARY

Of the total nitrogen of infants' feces, from 50 to 70 per cent. was found as proteins and amino acids, 2.4 to 24 per cent. as free amino acids, and from 3 to 37 per cent. as ammonia. Usually, though not invariably, the higher percentages of amino acid nitrogen were found in the looser stools, quicker passage through the intestine resulting in somewhat less complete absorption of these protein digestion products.

The results show no evidence of antagonism between the processes of acid and ammonia formation respectively in the intestine.

Urea was certainly absent in three-fourths of the stools examined, and in the other fourth formed only from 1 to 5.6 per cent. of the total nitrogen. Despite the care taken to keep the feces free from urine, we do not feel certain that at least a part of the few positive results may not have been due to the admixture of traces of urine. As some even of the watery stools contained no urea, it appears improbable that the intestine is capable of rendering significant assistance to the kidney, at least in the excretion of urea.

PROGRESS IN PEDIATRICS

PROGRESS IN OTOTOLOGY

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Were progress in otology to be reviewed from the standpoint of new discoveries during the past year, there might be but little to record; and even if there had been numerous inventions, there still would be but little at this time to relate or to advise concerning their importance as progressive factors.

Medical progress in any line is not a matter of innovations so much as it is degree in the dissemination of methods and principles that through careful analysis and thorough investigation have proven worthy of adoption. In that sense, then, it is probable that greater advancement has been made in the subject of otology during the past year than in any like period before. The past decade has marked a particularly active period in the recognition by specialist and general practitioner alike of important facts pertaining to the care of ears, points in prophylaxis, early recognition of pathologic processes and safety precautions in the course of their treatment. But the burden of responsibility for the preservation of the sense of hearing rests more heavily on the family physician or the pediatricist, whose position is that of chief adviser through the years of greatest susceptibility to ear infections. Probably nine-tenths of all cases of acquired deafness that come under the specialist's care in their adult years originated in childhood from preventable causes.

Middle ear suppurations, which have so frequently complicated the acute infectious diseases of children, we have learned, are indeed rare if the child's nares are kept freely open and cleansed by the careful employment of mild astringent applications to the turgescient mucous membrane, and the nasopharynx is kept clear of all accumulating mucous discharges. All cleansing technic in the course of acute processes should include only such agents as are capable of being applied with pledgets of cotton rather than forced sprays or irrigations of watery solutions in the nose and nasopharynx, which have doubtless caused more ear infections than they have ever prevented. The nasal douche, the safest of all irrigating methods, should be employed only after the swollen intranasal membrane has been reduced by astringent applications, and even then with greatest care if there be a purulent discharge from any accessory sinus.

One of the most important factors working to-day toward the insurance of good ears for the next generation, or all future generations, is the widespread or almost universal recognition of the effects of toxic absorption from necrotic tonsils and the consequent necessity of tonsillar enucleation as early in childhood as the diseased conditions are observed. Surely some one, and at some not far distant day, we trust, will discover a reason for the almost universal degenerative process which invades the faucial tonsils, most frequently in childhood, yet from which no age is immune, causing the secretion in the crypts to coagulate and become the highly toxic necrotic concretions that, reabsorbed, pass into the lymphatics to poison not only the contiguous tissues, but to affect vital functions throughout the body. Whatever might have been the gland's original function, it is lost or at best suspended in the presence of such a pathologic condition, and the dangers of retention are too great to warrant too prolonged attempts at restoration; so there is left but the one satisfactory alternative, enucleation. Even chronic aural discharges are frequently found to cease within a few days after the enucleation of tonsils that were perhaps so small that their necrotic state was for a long time unsuspected; in fact, it is the hidden, submerged, *retention* tonsil, regardless of its size, that is capable of the greatest damage to the ears. Remnants of tonsils, left in the fossae by incomplete operations, are also capable of prolonging all the ill effects that the original whole tonsil had created, which fact might explain myriads of disappointments where tonsils were supposed to have been removed. Pathologic enlargement of adenoid tissue in the nasopharynx, always an important factor in the interference of aural function, is probably due in most cases to toxic absorption from necrotic tonsils; hence the recurrence of adenoids in cases in which the removal of tonsils was either not attempted, or else attempted and not perfectly accomplished. Acute suppurative ethmoiditis is one of the most frequent sources of otitis media and should be guarded against in all severe or supposed prolonged "colds in the head." Every purulent nasal discharge, with but few exceptions, is from one or more of the accessory sinuses and demands immediate attention.

In the treatment of suppurative sinus and otitic infections one of the most important advances in recent years is vaccine therapy, to which the past year's testimony adds strong support. Difficulties attending the procuring of perfect autogenous vaccines have brought about the stock products which are now in most general use. Arguments against the use of the mixed vaccines have been refuted by clinical results, for when used in conjunction with and not as a substitute for the usual local and constitutional measures as employed by the up-to-

date aurist and rhinologist, the course of disease in an average case seems to be shortened by at least one-half, while even in those in which no benefit is observed, no harmful effects can be detected. A measure, then, that can be employed with probable benefit in 75 per cent. of all suppurative processes in the nasal accessory cavities or in those of the temporal bone, with a reasonable assurance that at least no harm will result from its use in the other 25 per cent., is indeed a safe and valuable remedy and is to be regarded as one of the most important advances of the age. Conservatism in the treatment of mastoiditis has been gaining ground for the past ten years, and particularly so with the more general adoption of vaccine therapy. The day may not be far distant when the radical mastoid operation will be a rare occurrence even in chronic suppurations, and entirely unnecessary in acute or subacute involvements. This change is being brought about by a more widespread knowledge concerning the treatment of conditions that lead to mastoid disease and by the improved means at our command for the treatment of the fully developed complication. Vaccine therapy is to-day one of the most potent instruments in the hand of preventive medicine, not so much in the sense of an immunizer against the primary invasion of disease-producing bacteria, but rather as a means of cutting off their advance into other surrounding and probably more vital tissues. In no part of the body is this more true or more evident than in the nose and throat where an unchecked apparently simple infection may lead to a serious impairment of one or all of the special senses, smell, taste, hearing and sight.

With the prevention or cure, then, of local infections that might eventually lead to middle ear suppuration, there is also prevented a large percentage of intracranial abscesses and meningeal complications.

During the past year there has continued some most creditable original research in disease of the labyrinth and methods of treatment. Such involvements, however, are more difficult of detection, require more intricate technic in treatment than the majority of diseases affecting only the middle and outer ear, and come only within the province of the skilled specialist, though every practitioner should remember that suppurative disease of the labyrinth is always secondary to an acute or chronic otitis media, and is apt to be accompanied by sudden, total and permanent deafness.

Indiscriminate efforts to inflate the middle ear, however attempted, or for whatever purpose practiced, is a process capable of marked and lasting injury to the ears and can not be too frequently nor too severely criticized. The forcing of air or other vapors into or through the eustachian tube, is a safe procedure only when the physician has thoroughly prepared the nares, nasopharynx and pharynx for its introduction, and even then its indications are exceedingly rare.

The employment of bougies for reestablishing a clear opening through the eustachian tube and to preserve its integrity has in a large measure been disappointing.

But in the treatment of chronic, nonsuppurative catarrhal lesions of the ears the greatest patience is required at all times, for even under most favorable circumstances results come slowly, and to know just how long a certain line of treatment should be persisted in or when discarded, is still at times a perplexing problem and some things must be recognized as impossible of accomplishment.

A popular impression with the laity and not infrequently among physicians that little or nothing can be done in the way of treatment for deafness has been established from erroneous opinions or absolute ignorance regarding the varieties of deafness and the various causes leading thereto. Such an opinion is harmful, in that it leads to neglect through the stages when relief might readily be obtained. The majority of cases of defective hearing are of a slowly progressive type, due to causes easily removable or perfectly amenable to cure in the earlier stages of auditory disturbance.

The organ of hearing is indeed a wonderfully delicate mechanism and capable of easy and irreparable injury, for which very reason nature seems to have placed it in the most perfectly fortified position. The eustachian tube and the external auditory canal are practically the only two roads open to attacks by infection and the latter of these but slightly exposed. If, then, there can be brought about a more concerted effort on the part of specialists and family physicians to educate the laity to the fact that nearly all diseases of the ear are secondary to infections in the nose and throat, that the earliest symptom of an ear involvement should serve as an alarm to seek immediate relief, and that "deafness can best be cured by being prevented," future generations will hear and regard as selfevident truths, principles and precautions which we have been slow to understand and still less willing to adopt.

The following list is not intended to be a complete index of the past year's literature on otology, but as representative selections bearing some relation to the subject in its various phases. From these herein given, however, one can not help but be impressed with the deep interest thus manifested, which in itself is one of the most potent factors for progress.

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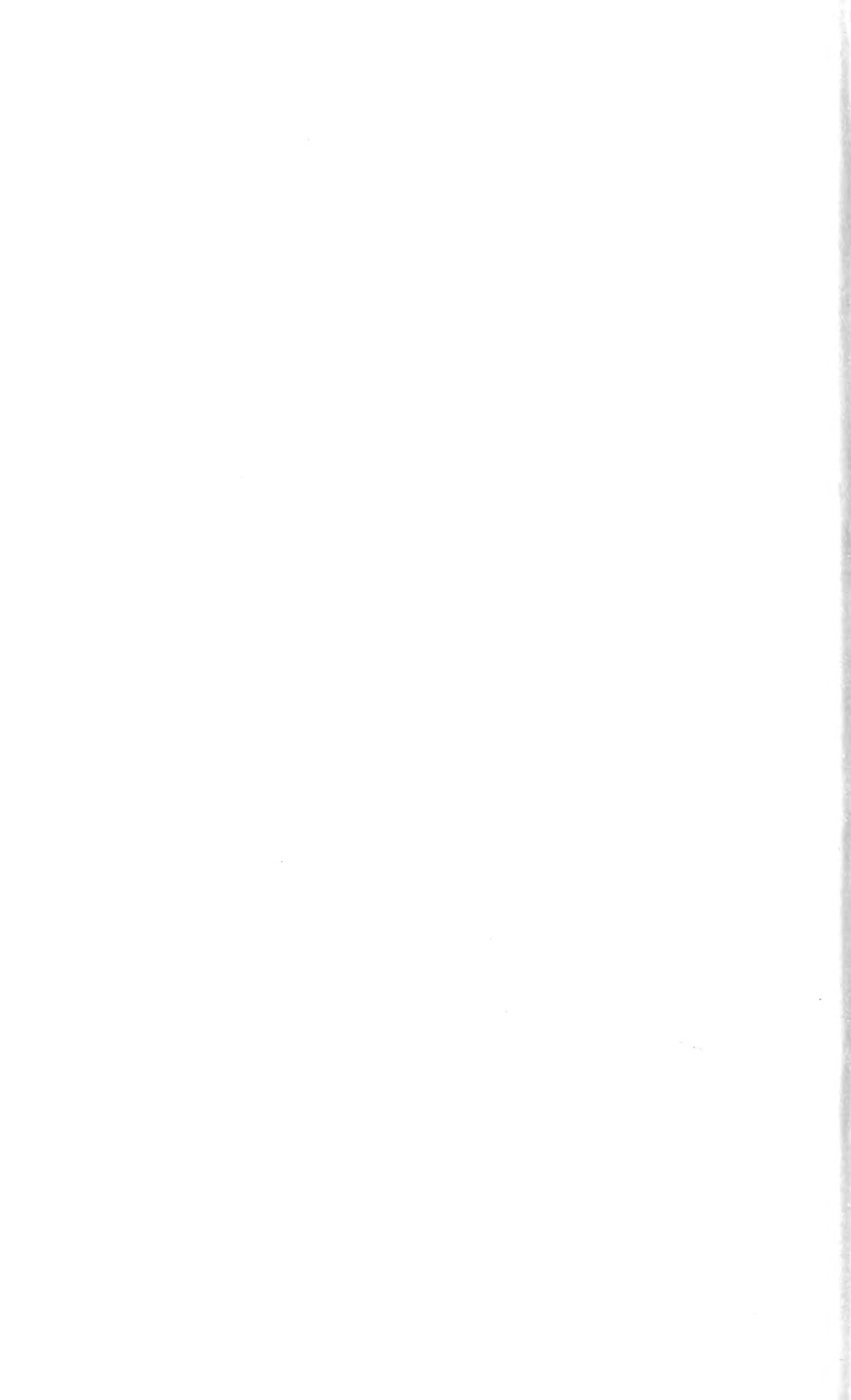
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